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UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-K

(Mark One)

☒ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**
For the fiscal year ended December 31, 2021
OR

☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**
For the transition period from to
Commission File No. 001-36033

THERAVANCE BIOPHARMA, INC.

(Exact name of registrant as specified in its charter)

Cayman Islands (State or Other Jurisdiction of Incorporation or Organization)	**98-1226628** (I.R.S. Employer Identification No.)
P.O. Box 309 **Ugland House, South Church Street** **George Town, Grand Cayman, Cayman Islands** (Address of Principal Executive Offices)	**KY1-1104** (Zip Code)

Registrant's telephone number, including area code: **650-808-6000**

SECURITIES REGISTERED PURSUANT TO SECTION 12(b) OF THE ACT:

Title of each class	**Trading Symbol**	**Name of each exchange on which registered**
Ordinary Share $0.00001 Par Value	TBPH	The Nasdaq Global Market

SECURITIES REGISTERED PURSUANT TO SECTION 12(g) OF THE ACT: **NONE**

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes ☒ No ☐

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act. Yes ☐ No ☒

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes ☒ No ☐

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§ 232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files). Yes ☒ No ☐

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large Accelerated Filer ☒	Accelerated Filer ☐
Non-accelerated Filer ☐	Smaller reporting company ☐
	Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Indicate by check mark whether the registrant has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report. ☒

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). Yes ☐ No ☒

The aggregate market value of the voting and non-voting common equity held by non-affiliates of the registrant was approximately $882.1 million, based upon the closing price of $14.52 on the Nasdaq Global Market on June 30, 2021.

On February 21, 2022, there were 74,696,687 of the registrant's ordinary shares outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Specified portions of the registrant's definitive Proxy Statement to be issued in conjunction with the registrant's 2022 Annual Meeting of Shareholders, which is expected to be filed not later than 120 days after the registrant's fiscal year ended December 31, 2021, are incorporated by reference into Part III of this Annual Report. Except as expressly incorporated by reference, the registrant's Proxy Statement shall not be deemed to be a part of this Annual Report on Form 10-K.

THERAVANCE BIOPHARMA, INC.
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PART I

Special Note regarding Forward-Looking Statements

This Annual Report on Form 10-K contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended (the "Securities Act"), and Section 21E of the Securities Exchange Act of 1934, as amended (the "Exchange Act"). Such forward-looking statements involve risks, uncertainties and assumptions. All statements in this Annual Report on Form 10-K, other than statements of historical facts, including statements regarding our strategy, future operations, future financial position, future revenues, projected costs, prospects, plans, intentions, designs, expectations and objectives are forward-looking statements. The words "aim," "anticipate," "assume," "believe," "contemplate," "continue," "could," "designed," "developed," "drive," "estimate," "expect," "forecast," "goal," "indicate," "intend," "may," "mission," "opportunities," "plan," "possible," "potential," "predict," "project," "pursue," "represent," "seek," "suggest," "should," "target," "will," "would," and similar expressions (including the negatives thereof) are intended to identify forward looking statements, although not all forward looking statements contain these identifying words. These statements reflect our current views with respect to future events or our future financial performance, are based on assumptions, and involve known and unknown risks, uncertainties and other factors which may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements. We may not actually achieve the plans, intentions, expectations or objectives disclosed in our forward-looking statements and the assumptions underlying our forward-looking statements may prove incorrect. Therefore, you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions, expectations and objectives disclosed in the forward-looking statements that we make. Factors that we believe could cause actual results or events to differ materially from our forward-looking statements include, but are not limited to, those discussed in "Risk Factors," in Item 1A, "Management's Discussion and Analysis of Financial Condition and Results of Operations" in Item 7 and elsewhere in this Annual Report on Form 10-K. Our forward-looking statements in this Annual Report on Form 10-K are based on current expectations and we do not assume any obligation to update any forward-looking statements for any reason, even if new information becomes available in the future. In addition, while we expect the effects of COVID-19, including new variants, to continue to adversely impact our business operations and financial results, the extent of the impact on our ability to generate revenue from YUPELRI® (revefenacin), our clinical development programs, and the value of and market for our ordinary shares, will depend on future developments that are highly uncertain and cannot be predicted with confidence at this time. These potential future developments include, but are not limited to, the ultimate duration of the COVID-19 pandemic, travel restrictions, quarantines, vaccination levels, social distancing and business closure requirements in the United States and in other countries, other measures taken by us and those we work with to help protect individuals from contracting COVID-19, and the effectiveness of actions taken globally to contain and treat the disease, including vaccine availability, distribution, acceptance and effectiveness. When used in this report, all references to "Theravance Biopharma", the "Company", or "we" and other similar pronouns refer to Theravance Biopharma, Inc. collectively with its subsidiaries.

PART I

ITEM 1. BUSINESS

Overview

Theravance Biopharma, Inc. ("we," "our," "Theravance Biopharma" or the "Company") is a biopharmaceutical company primarily focused on the discovery, development and commercialization of respiratory medicines. Our core purpose is to create *medicines that make a difference*® in people's lives.

In pursuit of our purpose, we leverage decades of respiratory expertise to discover and develop transformational medicines that make a difference. These efforts have led to the development of the United States ("US") Food and Drug Administration (the "FDA") approved YUPELRI® (revefenacin) inhalation solution indicated for the maintenance treatment of patients with chronic obstructive pulmonary disease ("COPD"). Our respiratory pipeline of internally discovered programs is targeted to address significant patient respiratory needs.

We have an economic interest in potential future payments from Glaxo Group or one of its affiliates ("GSK") pursuant to our agreements with Innoviva, Inc. ("Innoviva") relating to certain programs, including TRELEGY.

2021 Significant Developments

Financing

We successfully closed an offering of 7,705,000 ordinary shares at a price to the public of $15.00 per share in June 2021 raising $115.6 million, before deducting underwriting discounts and commissions and offering expenses. The net proceeds from the offering are intended to support the development of our clinical product candidates and for general working capital purposes.

Clinical Results from Late-Stage Studies of Izencitinib and Ampreloxetine

In August 2021, we reported that results from our Phase 2b dose-finding induction study of izencitinib, our oral gut-selective pan-JAK inhibitor for inflammatory intestinal diseases, previously partnered with Janssen Biotech, Inc. ("Janssen"), did not meet its primary endpoint of change in the total Mayo score or the key secondary endpoint of clinical remission at week 8, relative to placebo.

In addition, in September 2021, we reported that results from our four-week Phase 3 study (SEQUOIA) of ampreloxetine, our norepinephrine reuptake inhibitor, did not meet its primary endpoint for assessing safety and efficacy compared to placebo for the treatment of symptomatic neurogenic orthostatic hypotension ("nOH").

Strategic Actions to Focus on Respiratory Diseases

Given the above clinical results, in September 2021, our board of directors approved a plan to focus our resources on our most promising respiratory programs and reduce the size of the Company in order to maximize shareholder value. At completion, the corporate restructuring (the "Restructuring") will result in us reducing headcount by approximately 75%, an estimated 270 positions, through a reduction in our workforce. Approximately 75% of the total reduction in workforce occurred at the end November 2021, and the remainder will be completed at the end of February 2022.

As a result of the Restructuring, we expect to realize estimated operating expense savings (excluding share-based compensation and any one-time restructuring, severance, and termination costs) of approximately $170.0 million. We estimate that we will incur total Restructuring and related expenses of approximately $32.0 million comprised of $17.0 million in cash expenses associated with employee termination benefits and related costs and $15.0 million in non-cash expenses relating to the acceleration of equity-awards for employees affected by the Restructuring. In 2021, we recognized $20.1 million of the Restructuring expenses comprised of $11.5 million in cash-related expenses and $8.6 million in non-cash expenses.

We expect to recognize the majority of the remaining Restructuring and related expenses of approximately $12.0 million, comprised of $5.0 million in cash-related expenses and $7.0 million in non-cash expenses, in the first quarter of 2022 and the balance by the third quarter of 2022. The remaining Restructuring expense estimates are subject to a number of assumptions, and actual final amounts may differ. We may also incur additional costs not currently contemplated due to events that may occur as a result of, or that are associated with, the Restructuring.

The go-forward organization leverages our expertise in developing and commercializing respiratory therapeutics. We intend to significantly narrow our R&D focus on our core respiratory assets, including a clinical study with Viatris Inc. ("Viatris") intended to provide data to support a possible label update for YUPELRI, which we believe would capture more of YUPELRI's addressable market and further strengthen its competitive advantage, and investment in our inhaled Janus kinase inhibitor portfolio, with focus on our most advanced clinical candidate, nezulcitinib, initially targeting acute lung injury. We will also continue to explore strategic partnerships for both core and non-core assets to unlock value. All of these actions drive towards our goal to maximize shareholder value.

After implementing these strategic actions, we plan to become sustainably cash flow positive beginning in the second half of 2022, and we will work to optimize our capital structure in order to maximize total shareholder returns.

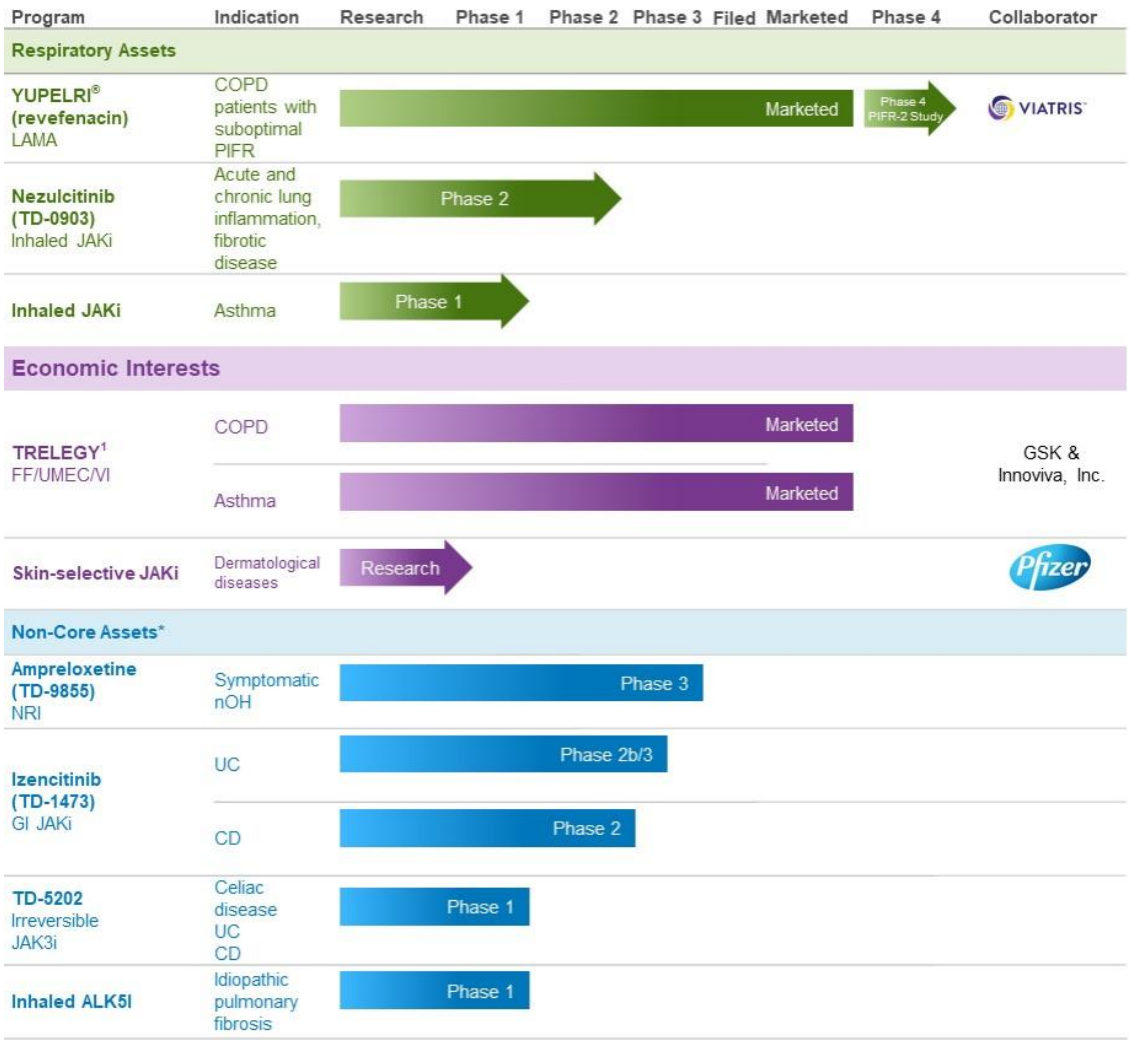
Impact of COVID-19 Pandemic

The effects of the COVID-19 pandemic and the related actions by governments, companies, and individuals around the world in an attempt to contain the spread of the virus (including new variants of COVID-19) continue to present a substantial public health and economic challenge and are affecting our employees, patients, communities, clinical trial sites, suppliers, business partners and business operations. The full extent to which the COVID-19 pandemic will continue to directly or indirectly impact our business, results of operations and financial condition, including revenue, expenses, clinical trials and research and development costs, will depend on future developments that are highly uncertain and may be impacted by the emergence of new information concerning the COVID-19 pandemic, ongoing spread of the disease across the US and the globe, and the actions taken to contain or treat the disease, including vaccine availability, distribution, acceptance and effectiveness.

As part of our response to the ongoing COVID-19 pandemic, we have taken steps to identify and mitigate the adverse impacts on, and risks to, our business posed by its spread and actions taken by governmental and health authorities to address the COVID-19 pandemic. We expect to continue to implement measures as may be required or recommended by government authorities or as we determine are in the best interests of our employees, clinical trial sites and participants, the patients we serve, and other stakeholders in light of COVID-19.

Our Programs

The table below summarizes the status of our approved product and our other product candidates in development. The table also includes the status of the respiratory programs in which we have an economic interest and for which GSK is responsible pursuant to agreements between Innoviva and GSK ("GSK-Partnered Respiratory Programs"). These programs consist primarily of the TRELEGY program. We have an economic interest in these programs through our interest in Theravance Respiratory Company, LLC ("TRC"), a limited liability company managed by Innoviva. The status of all GSK-Partnered Respiratory Programs referenced in this Annual Report on Form 10-K are based solely upon publicly available information and may not reflect the most recent developments under the programs.



(1) We hold an 85% economic interest in upward-tiering royalty stream of 6.5% – 10% payable by GSK (net of TRC expenses paid and the amount of cash, if any, expected to be used by TRC pursuant to the TRC LLC Agreement over the next four fiscal quarters). 75% of TRC royalties received are pledged to service outstanding notes, and 25% of royalties received are retained by us. All statements concerning TRELEGY are based on publicly available information.

* Limited additional capital investment planned after the first quarter of 2022.

Glossary of Defined Terms used in Table Above:

COPD: Chronic Obstructive Pulmonary Disease;
CD: Crohn's Disease;
FF: Fluticasone Furoate;
JAKi: Janus Kinase Inhibitor;
LAMA: Long-Acting Muscarinic Antagonist;
nOH: Neurogenic Orthostatic Hypotension;
NRI: Norepinephrine Reuptake Inhibitor;
UC: Ulcerative Colitis;
UMEC: Umeclidinium; and
VI: Vilanterol

Respiratory Program Highlights

YUPELRI (revefenacin) Inhalation Solution

YUPELRI (revefenacin) inhalation solution is a once-daily, nebulized long-acting muscarinic antagonist ("LAMA") approved for the maintenance treatment of COPD in the US. LAMAs are recognized by international COPD treatment guidelines as a cornerstone of maintenance therapy for COPD, regardless of severity of disease. Our market research indicates there is an enduring population of COPD patients in the US that either need or prefer nebulized delivery for maintenance therapy. The stability of revefenacin in both metered dose inhaler and dry powder inhaler ("MDI/DPI") formulations suggests that revefenacin could also serve as a foundation for novel handheld combination products.

In November 2018, YUPELRI was approved by the FDA for the maintenance treatment of patients with COPD. Following shipments into commercial channel in late 2018, we and our collaboration partner, Viatris, formally launched our sales and marketing efforts in early 2019. In 2020 and through 2021, YUPELRI's growth trajectory was impacted by the COVID-19 pandemic. However, in late 2021, we began to observe a return to growth in YUPELRI sales. We continue to monitor the impact of the ongoing COVID-19 pandemic on demand for YUPELRI, including the duration and degree to which we may see the rate of starting new patients on YUPELRI and customer orders return to pre-pandemic levels. Although we believe there are signals of easing pandemic restrictions, at this time, we are unable to predict with certainty the ultimate disruptive impact of the ongoing COVID-19 pandemic on YUPELRI, but it is possible the pandemic may continue to put downward pressure on our sales. As a result, the observed sales volatility may continue into 2022.

We and Viatris continue to supply YUPELRI to our patients and currently do not anticipate any interruptions in supply. In addition, we are tracking several key performance metrics to gauge success in building market acceptance, including formulary success and market access.

In August 2021, we announced that in collaboration with our partner Viatris, we are initiating a Phase 4 study comparing improvements in lung function in adults with severe to very severe COPD and suboptimal inspiratory flow rate following once-daily treatment with either YUPELRI delivered via standard jet nebulizer or tiotropium delivered via a dry powder inhaler (Spiriva® HandiHaler®). This study is aimed at helping to better inform decisions when physicians are designing a personalized COPD treatment plan with patients and is intended to support a possible label update for YUPELRI, which would capture more of YUPELRI's addressable market and further strengthen its competitive advantage. In January 2022, we announced the enrollment of the first patient in the Phase 4 study.

Viatris Collaboration

In January 2015, we and Viatris established a strategic collaboration for the development and commercialization of revefenacin. Partnering with a leader in nebulized respiratory therapies enables us to expand the breadth of our revefenacin development program and extend our commercial reach beyond the acute care setting. Viatris funded the Phase 3 development program of YUPELRI, enabling us to advance other high value pipeline assets

alongside YUPELRI.

Under the terms of the Viatris Development and Commercialization Agreement (the "Viatris Agreement"), Viatris and Theravance Biopharma co-develop revefenacin for COPD and other respiratory diseases. We led the US Phase 3 development program for YUPELRI in COPD, and Viatris was responsible for reimbursement of our costs related to the registrational program up until the approval of the first new drug application ("NDA"), after which costs are shared. With YUPELRI approved in the US, Viatris is leading commercialization, and we co-promote the product in the US under a profit and loss sharing arrangement (65% to Viatris; 35% to Theravance Biopharma). Outside the US, Viatris is responsible for development and commercialization and will pay us a tiered royalty on net sales at percentage royalty rates ranging from low double-digits to mid-teens.

In June 2019, we announced the expansion of the Viatris Agreement to grant Viatris exclusive development and commercialization rights to nebulized revefenacin in China and adjacent territories, which include Hong Kong SAR, the Macau SAR, and Taiwan. In exchange, we received an upfront payment of $18.5 million (before a required tax withholding) and will be eligible to receive additional potential development and sales milestones totaling $54.0 million and low double-digit tiered royalties on net sales of nebulized revefenacin, if approved. In March 2020, we earned a $1.5 million development milestone for the acceptance of a clinical trial application associated with the use of revefenacin monotherapy in China and adjacent territories. Viatris is responsible for all aspects of development and commercialization in the partnered regions, including pre- and post-launch activities and product registration and all associated costs. We retain worldwide rights to revefenacin delivered through other dosage forms, such as a MDI/DPI.

Under the Viatris Agreement, as of December 31, 2021, we are eligible to receive from Viatris potential global development, regulatory and sales milestone payments totaling up to $257.5 million in the aggregate with $205.0 million associated with YUPELRI monotherapy and $52.5 million associated with future potential combination products. Of the $205.0 million associated with monotherapy, $187.5 million relates to sales milestones based on achieving certain levels of net sales and $17.5 million relates to global development and regulatory actions. The $52.5 million associated with future potential combination products relates solely to global development and regulatory actions.

Lung-selective, Nebulized Pan-Janus Kinase (JAK) Inhibitor (Nezulcitinib)

Nezulcitinib (formerly known as TD-0903) is a lung-selective, nebulized JAK inhibitor, in clinical development for the potential treatment of hospitalized patients with Acute Lung Injury ("ALI") caused by COVID-19. We discovered nezulcitinib, and it has been shown in experimental murine models to have potent, broad inhibition of JAK-STAT signaling in the airways following challenges with multiple cytokines. Preclinical studies suggest that nezulcitinib has a high lung to plasma ratio and rapid metabolic clearance resulting in low systemic exposure, compatible with its lung selectivity. Nezulcitinib is administered via nebulized inhalation solution, which further enhances its lung selectivity. Preclinical pharmacodynamic studies indicate that nezulcitinib has an extended duration of action that should enable once daily dosing in humans.

We believe nezulcitinib has the potential to inhibit the cytokine storm associated with ALI and prevent progression to Acute Respiratory Distress Syndrome ("ARDS"). The first healthy volunteer was dosed in a Phase 1 study of nezulcitinib in April 2020, and in June 2020, we completed Phase 1 and entered a two-part Phase 2 study. Phase 2 was designed to evaluate the efficacy, safety, and tolerability of nezulcitinib in subjects with confirmed symptomatic COVID-19 hospitalized for symptomatic respiratory insufficiency. This study also evaluated the PK of nezulcitinib in these subjects. To expedite enrollment, we opened additional sites in other regions including Europe, the US, and South America.

We completed Phase 2, Part 1, a small sub-study of 25 patients intended to assess safety, PK and exploratory clinical measures of three doses of nezulcitinib versus placebo. Data showed that inhaled administration of nebulized nezulcitinib, once daily over seven days, was generally well-tolerated and showed a numerical trend towards improved clinical status, reduced hospital stay and resulted in fewer deaths compared to placebo during a 28-day observation period. Nezulcitinib also demonstrated evidence of improvements in several relevant inflammatory biomarkers and low systemic exposure at all doses. This demonstrates the lung-selective design features of the molecule.

The Phase 2 Dose Finding study was a randomized, double-blind, parallel-group study evaluating efficacy and safety of one dose (3 mg) of nezulcitinib (selected based on the data from Part 1) as compared with placebo in 200 patients. In June 2021, we announced top-line results from our Phase 2 study of 3 mg once-daily nezulcitinib compared to placebo, each in combination with standard of care, which generally included steroids. The study did not meet the primary endpoint of number of Respiratory Failure-Free Days from randomization through Day 28 in the intent-to-treat population. The study also did not meet secondary endpoints, with no difference shown in change from baseline at Day 7 in SaO_2/FiO_2 ratio, proportion of patients in each category of the eight-point Clinical Status scale, or proportion of patients alive and respiratory failure-free at Day 28. However, nezulcitinib demonstrated a favorable trend in improvement when compared to placebo for 28-day all-cause mortality. In addition, in a post-hoc analysis of patients with C-reactive protein ("CRP") <150 mg/L, there was an improvement in those treated with nezulcitinib when compared to placebo in 28-day all-cause mortality and in time to recovery while there was no difference in these outcomes in patients with CRP >150 mg/L. Nezulcitinib was generally well-tolerated, and we intend to further investigate its therapeutic potential as part of our newly focused respiratory portfolio.

Lung-selective Pan-JAK Inhibitor Program

TD-8236, an inhaled lung-selective pan-JAK inhibitor, demonstrated a high affinity for each of the JAK family of enzymes (JAK1, JAK2, JAK3 and TYK2) that play a key role in cytokine signaling. Inhibiting these JAK enzymes interferes with the JAK/STAT signaling pathway and, in turn, modulates the activity of a wide range of pro-inflammatory cytokines. While orally-administered JAK inhibitors are currently approved for the treatment of a range of inflammatory diseases, no inhaled JAK inhibitor is approved for the treatment of airway disease, including asthma. The pan-JAK activity of TD-8236 suggests that it may impact a broad range of cytokines that have been associated both T2-high and T2-low asthma. Many moderate to severe asthma patients comprising both T2 phenotypes remain symptomatic despite being compliant on high doses of inhaled steroids. Importantly, TD-8236 was designed to distribute and exert its anti-inflammatory effect within the lungs following dry powder inhalation, with the potential to treat inflammation within that organ while minimizing systemic exposure. In preclinical assessments, TD-8236 has shown to potently inhibit targeted mediators of T2-high and T2-low asthma in human cells.

In September 2019, we announced positive results from a Phase 1 single-ascending dose and multiple-ascending dose clinical trial of TD-8236, an investigational, inhaled lung-selective pan-JAK inhibitor that has demonstrated a high affinity for each of the JAK family of enzymes (JAK1, JAK2, JAK3 and TYK2) that play a key role in cytokine signaling. The Part C extension portion of the Phase 1 trial, assessing additional biomarkers in patients with moderate to severe asthma, demonstrated that biomarkers of JAK target engagement (including exhaled nitric oxide and pSTAT1 and pSTAT6 in cellular fractions of bronchoalveolar lavage fluid) were reduced after 7 days of once-daily dosing at a dose level of 1500 µg. In December 2019, we announced the initiation of a Phase 2 allergen challenge study of TD-8236 in mild allergic asthma patients, and we reported results of the Phase 1C study in the third quarter of 2020. TD-8236 is the first JAK inhibitor to be studied in a Phase 2a Lung Allergen Challenge ("LAC") study, but inconsistent with our expectations, it had no impact on decrease in lung function (FEV1) following allergen inhalation after 14 days of once-daily dosing at dose levels of 150 µg and 1500 µg compared to placebo and did not meet the primary study objective. The collective data set (preclinical, Phase 1, Phase 2a) demonstrates TD-8236 engages the JAK mechanism at a dose of 1500 µg as evidenced by the reduction in FeNO and reductions in pSTAT, but does not protect against the lung function decline seen after allergen inhalation.

After completing additional analysis on TD-8236 gene signature and biomarker data from the Phase 1C study, we found that the data are consistent with target engagement in the lung. However, based on our current understanding of TD-8236, we have decided to pause the clinical program for this compound in its current form and apply our learnings to refining and expanding molecules in our portfolio of inhaled JAK inhibitors. We expect to proceed into the clinic with the next generation compound after securing a strategic partnership.

The robust body of scientific evidence from TD-8236 and nezulcitinib programs provide confidence for us to continue the lung-selective inhaled JAK inhibitor program for asthma. The full data set for TD-8236 will be presented at future scientific meetings.

Non-Core Asset Highlights

The key operational activities for all izencitinib and ampreloxetine studies will be completed by the end of the first quarter of 2022.

Ampreloxetine (TD-9855)

Ampreloxetine is an investigational, once-daily norepinephrine reuptake inhibitor ("NRI") that we were developing for the treatment of patients with symptomatic neurogenic orthostatic hypotension ("nOH"). nOH is caused by primary autonomic failure conditions, including multiple system atrophy, Parkinson's disease and pure autonomic failure. The compound has high affinity for binding to norepinephrine transporters. By blocking the action of these transporters, ampreloxetine causes an increase in extracellular concentrations of norepinephrine. Ampreloxetine is wholly owned by Theravance Biopharma.

Based on positive top-line four-week results from a small exploratory Phase 2 study in nOH and discussions with the FDA, we advanced ampreloxetine into a Phase 3 program. We announced the initiation of patient dosing in study in early 2019. The Phase 3 program consists of two pivotal studies and one non-pivotal study. The first pivotal study (SEQUOIA), a four-week, randomized double-blind, placebo-controlled study, was designed to evaluate the efficacy and safety of ampreloxetine in patients with symptomatic nOH. The second pivotal study (REDWOOD), a four-month open label study followed by a six-week randomized withdrawal phase was designed to evaluate the durability of patient response of ampreloxetine. The third, non-pivotal study (OAK), was designed to allow patients who completed REDWOOD to have continued access to ampreloxetine for up to three and half years.

In September 2021, we reported that the four-week SEQUOIA Phase 3 clinical study did not meet its primary endpoint. Most treatment-related adverse events were mild or moderate in severity. Serious adverse events occurred in two patients on placebo and four on ampreloxetine and none were considered related to the study drug. No deaths were reported, and there was no signal for supine hypertension. Study activities for the ampreloxetine Phase 3 program will be completed by the end of the first quarter of 2022.

Gut-selective Pan-JAK Inhibitor Program (Izencitinib)

JAK inhibitors function by inhibiting the activity of one or more of the Janus kinase family of enzymes (JAK1, JAK2, JAK3, TYK2) that play a key role in cytokine signaling. Inhibiting these JAK enzymes interferes with the JAK/STAT signaling pathway and, in turn, modulates the activity of a wide range of pro-inflammatory cytokines. JAK inhibitors are currently approved for the treatment of rheumatoid arthritis, myelofibrosis, atopic dermatitis, and ulcerative colitis and have demonstrated therapeutic benefit for patients with Crohn's disease. However, these products are known to have side effects based on their systemic exposure. With izencitinib, our goal was to develop an orally administered, gut-selective pan-JAK inhibitor specifically designed to distribute adequately and predominantly to the tissues of the intestinal tract, treating inflammation in those tissues while minimizing systemic exposure.

Based on positive results from a Phase 1b exploratory study in ulcerative colitis and following dialogues with the FDA and European Medicines Agency ("EMA") regarding study design, we advanced izencitinib into two clinical studies in inflammatory intestinal diseases. The Phase 2 (DIONE) study was a twelve-week randomized, double-blind, placebo-controlled study designed to evaluate the efficacy and safety of patients with Crohn's disease, which began dosing patients in late 2018. The Phase 2b/3 (RHEA) study was a randomized, double-blind, placebo-controlled study to evaluate the efficacy and safety of eight weeks induction and 44 weeks maintenance therapy in patients with ulcerative colitis, which began dosing patients in early 2019.

In August 2021, we reported that the Phase 2b/3 (RHEA) study did not meet its primary endpoint of change in the total Mayo score or the key secondary endpoint of clinical remission at week 8, relative to placebo. There was a small dose-dependent increase in clinical response measured by the adapted Mayo score, which was driven by a reduction in rectal bleeding.

At all doses, izencitinib was well-tolerated when administered orally once daily for 8 weeks; adverse event rates were similar among patients receiving izencitinib and placebo. There were no instances of perforation, opportunistic

infection, major cardiovascular or thromboembolic event, complicated zoster, or non-melanoma skin cancer in patients receiving izencitinib. There were no notable changes in lab values including creatine phosphokinase and lipids in patients receiving izencitinib relative to placebo. Plasma exposure of izencitinib was low, consistent with expectations for a gut-selective medicine. We plan to present the study results at a future scientific forum. The Phase 2 study in Crohn's disease with izencitinib has completed enrollment with top-line results expected in the first quarter of 2022.

Irreversible JAK3 Inhibitor (TD-5202)

TD-5202 is an investigational, orally administered, gut-selective, irreversible JAK3 inhibitor that has demonstrated a high affinity for the JAK3 enzyme. Through the selective inhibition of JAK3, TD-5202 interferes with the JAK/STAT signaling pathway and, in turn, modulates the activity of select pro-inflammatory cytokines, including IL-2, IL-15, and IL-21 which play a central role in the pathogenesis of T-cell mediated disease, including inflammatory intestinal disease, such as celiac disease. Importantly, TD-5202 is specifically designed to act locally within the intestinal wall thereby limiting systemic exposure.

In September 2019, we announced the initiation of a Phase 1 single ascending dose and multiple ascending dose trial designed to evaluate the safety and tolerability of TD-5202 in healthy participants, plus assess plasma pharmacokinetics of TD-5202 to confirm circulating levels are low, consistent with a gut-selective approach. In February 2020, we announced that data from the Phase 1 study indicated that TD-5202 was generally well tolerated as a single oral dose up to 2000 milligrams and as a twice-daily oral dose up 2000 milligrams total per day given for ten consecutive days in healthy participants.

Janssen Biotech Collaboration

In February 2018, we announced a global co-development and commercialization agreement with Janssen for izencitinib and related back-up compounds for inflammatory intestinal diseases, including ulcerative colitis and Crohn's disease. Under the terms of the agreement, we received an upfront payment of $100.0 million and was eligible to receive up to an additional $900.0 million in potential payments, inclusive of a potential $200.0 million opt-in payment following completion of the Phase 2 Crohn's disease study and the Phase 2b induction portion of the ulcerative colitis study. Following the unfavorable Phase 2b ulcerative colitis study results announced in August 2021, in December 2021, we received notice from Janssen terminating the agreement, effective January 16, 2022.

Inhaled ALK5i

Our ALK5 inhibitor is a potential first-in-class, inhaled anti-fibrotic agent for the treatment of idiopathic pulmonary fibrosis ("IPF"), a fatal chronic lung disease with limited treatment options. Despite treatment with the current standard of care, IPF patients continue to experience disease progression and exacerbation, and therefore IPF treatment represents a significant unmet medical need. The compound targets the TGFβ pathway, a core signaling pathway that drives fibrosis. By being inhaled, the ALK5i efficiently inhibits TGFβ signaling locally in the lung which is expected to maximize its therapeutic effect.

Economic Interest in GSK-Partnered Respiratory Programs

We hold an 85% economic interest in any future payments that may be made by GSK to Theravance Respiratory Company, LLC ("TRC") pursuant to its agreements with Innoviva (net of TRC expenses paid and the amount of cash, if any, expected to be used by TRC pursuant to the TRC LLC Agreement over the next four fiscal quarters) relating to the GSK-Partnered Respiratory Programs, which Innoviva partnered with GSK and assigned to TRC in connection with Innoviva's separation of its biopharmaceutical operations into its then wholly-owned subsidiary Theravance Biopharma in June 2014. The GSK-Partnered Respiratory Programs consist primarily of the TRELEGY program, which is described in more detail below. We are entitled to this economic interest through our equity ownership in TRC. Our economic interest does not include any payments associated with RELVAR ELLIPTA/BREO ELLIPTA, ANORO ELLIPTA or vilanterol monotherapy.

The following information regarding the TRELEGY program is based solely upon publicly available information and may not reflect the most recent developments under the programs.

TRELEGY (the combination of fluticasone furoate/umeclidinium bromide/vilanterol)

TRELEGY provides the activity of an inhaled corticosteroid (FF) plus two bronchodilators (UMEC, a LAMA, and VI, a long-acting beta2 agonist, or LABA) in a single delivery device administered once-daily. TRELEGY is approved for use in the US, European Union ("EU"), and other countries for the long-term, once-daily, maintenance treatment of patients with COPD. We hold an 85% economic interest in the royalties payable by GSK to TRC on worldwide net sales (net of TRC expenses paid and the amount of cash, if any, expected to be used by TRC pursuant to the TRC LLC Agreement over the next four fiscal quarters) through our interest in TRC. Those royalties are upward-tiering from 6.5% to 10%, resulting in cash flows to us of approximately 5.5% to 8.5% of worldwide net sales of TRELEGY (net of TRC expenses paid and the amount of cash, if any, expected to be used by TRC pursuant to the TRC LLC Agreement over the next four fiscal quarters). Theravance Biopharma is not responsible for any of GSK's costs related to the development or commercialization of TRELEGY.

Additionally, the FDA approved an sNDA for the use of TRELEGY to treat asthma in adults in September 2020 making TRELEGY the first once-daily single inhaler triple therapy for the treatment of both asthma and COPD in the US. GSK has obtained approval for the asthma indication in ten additional markets. TRELEGY is currently expected to generate global peak sales of $3.6 billion annually according to consensus estimates. Over the past three years, TRELEGY has shown impressive growth, with global net sales increasing from $663 million in 2019 to $1.1 billion in 2020 and to $1.7 billion in 2021.

Theravance Respiratory Company, LLC

Prior to the June 2014 spin-off from Innoviva, our former parent company, Innoviva assigned to Theravance Respiratory Company, LLC ("TRC"), a Delaware limited liability company formed by Innoviva, its strategic alliance agreement with GSK and all of its rights and obligations under its collaboration agreement with GSK, other than with respect to RELVAR ELLIPTA/BREO ELLIPTA, ANORO ELLIPTA and vilanterol monotherapy.

Our equity interest in TRC is the mechanism by which we are entitled to the 85% economic interest in any future payments made by GSK under the strategic alliance agreement and under the portion of the collaboration agreement assigned to TRC by Innoviva (net of TRC expenses paid and the amount of cash, if any, expected to be used by TRC pursuant to the TRC LLC Agreement over the next four fiscal quarters). TRELEGY is currently the only commercial product arising out of the GSK agreements assigned by Innoviva to TRC. Royalty payments from GSK to TRC arising from the net sales of TRELEGY are presented in our consolidated statements of operations within "Income from investment in TRC, LLC" and is classified as non-operating income. In June 2020, we also recorded $8.5 million within "Income from investment in TRC, LLC" representing our share of a $10.0 million fee that GSK agreed to pay TRC upon termination of the inhaled Bifunctional Muscarinic Antagonist-Beta2 Agonist ("MABA") program. Seventy-five percent of the "Income from investment in TRC, LLC," as evidenced by the Issuer II Class C Units (defined below), is available only for payment of the $400.0 million original aggregate amount of 9.5% fixed rate non-recourse term notes due 2035 (the "Non-Recourse 2035 Notes") and is not available to pay our other obligations or the claims of our other creditors.

Our special purpose subsidiary Triple Royalty Sub II LLC (the "Issuer II") issued the Non-Recourse 2035 Notes in February 2020, the proceeds of which were used in part to repay the outstanding balance of our 9.0% non-recourse notes, due on or before 2033 (the "Non-Recourse 2033 Notes") that were issued in November 2018. The Non-Recourse 2035 Notes are secured by all of the Issuer II's rights, title and interest as a holder of certain membership interests (the "Issuer II Class C Units") in TRC. The Issuer II Class C Units entitle the Issuer II to receive 63.75% of the economic interest that TRC receives in any future payments made by GSK under the agreements described above, or 75% of the income from our 85% ownership interest in TRC.

We initiated an arbitration proceeding in October 2020 against Innoviva and TRC, challenging the authority of Innoviva and TRC to pursue a business plan to use TRELEGY royalties to invest in certain privately-held companies, rather than distribute such funds that would otherwise be available for distribution to us under the terms of the TRC LLC Agreement to us in a manner that we believe is consistent with the TRC LLC Agreement and our 85% economic interest in TRC.

On March 30, 2021, the arbitrator ruled that, we had not shown that at their then current levels of investment, Innoviva and TRC had not breached the TRC LLC Agreement as of the date of the arbitration. The arbitrator further ruled that Innoviva and TRC had not breached the implied covenant of good faith and fair dealing; or their fiduciary duties. The arbitrator also ruled that (i) Innoviva was entitled to indemnification from TRC for all legal fees and expenses reasonably incurred in the arbitration and (ii) we were entitled to indemnification from TRC for legal fees and costs incurred in defending an action Innoviva brought against us in the Delaware Court of Chancery. The arbitrator noted in the ruling that although we failed to show that Innoviva's investment activities, at the then current levels of investment, have or will have a material and adverse effect on our economic interest in TRC, this does not mean that any future investments or actions will not require our consent. The arbitrator noted in the ruling that we may, in the future, have a consent right over the decision to continue this investment strategy or whether to make a particular investment if, for example, Innoviva develops a track record of poor investments, over allocates royalties to these investment activities, or fails to distribute sufficient investment returns, and such facts cause the strategy or investment to have a material adverse effect on our economic interest in TRC.

Pursuant to the terms of the TRC LLC Agreement, Innoviva is required to deliver to us a draft quarterly financial plan 30 days prior to the end of each fiscal quarter covering the next fiscal quarter. While the TRC LLC Agreement provides that Innoviva must consider in good faith any comments the Company provides, an applicable financial plan becomes effective 30 days after the draft plan is provided to the Company. We have objected to the proposed investments in private companies presented in draft TRC quarterly financial plans to date. If TRC identifies and consummates investments and incurs associated fees identified in a TRC quarterly plan, even over the Company's objections, distributions by TRC to its members in subsequent quarters will be reduced.

Our objections with regard to a draft TRC quarterly plan or other actions by TRC could result in additional legal proceedings between us, TRC and Innoviva, as was the case when we initiated arbitration proceedings against Innoviva and TRC in May 2019 and again in October 2020. Any such legal proceedings could divert the attention of management and cause us to incur significant costs, regardless of the outcome, which we cannot predict. If such proceedings were pursued, there can be no assurance that they would result in us receiving additional distributions from TRC. An adverse result could materially and adversely affect the funds that our affiliates would otherwise expect to receive from TRC in the future. See *"Risk Factors—We do not control the commercialization of TRELEGY and we do not control TRC; accordingly the amount of royalties we receive will depend on, among other factors, GSK's ability to further commercialize TRELEGY and TRC's decisions concerning use of cash in accordance with the TRC LLC Agreement"* for additional information.

Other Economic Interests

Selective 5-HT4 Agonist (TD-8954)

TD-8954 is a selective 5-HT4 receptor agonist being developed for potential use in the treatment of gastrointestinal motility disorders.

Takeda Collaborative Arrangement

In June 2016, we entered into a License and Collaboration Agreement (the "Takeda Agreement") with Millennium Pharmaceuticals, Inc. ("Millennium"), in order to establish a collaboration for the development and commercialization of TD-8954 (TAK-954). Millennium is an indirect wholly-owned subsidiary of Takeda Pharmaceutical Company Limited ("Takeda"). TD-8954 is currently in a Phase 2 study as a potential treatment for post-operative gastrointestinal dysfunction. Under the terms of the Takeda Agreement, Takeda is responsible for worldwide development and commercialization of TD-8954. We received an upfront cash payment of $15.0 million and will be eligible to receive success-based development, regulatory and sales milestone payments from Takeda. We will also be eligible to receive a tiered royalty on worldwide net sales by Takeda at percentage royalty rates ranging from low double-digits to mid-teens.

Skin-selective Pan-JAK inhibitor Program

In December 2019, we entered into a global license agreement with Pfizer Inc. ("Pfizer") for our preclinical skin-selective, locally-acting pan-JAK inhibitor program (the "Pfizer Agreement"). The compounds in this program are

designed to target validated pro-inflammatory pathways and are specifically designed to possess skin-selective activity with minimal systemic exposure.

Under the Pfizer Agreement, Pfizer has an exclusive license to develop, manufacture and commercialize certain compounds for all uses other than gastrointestinal, ophthalmic and respiratory applications. We received an upfront cash payment of $10.0 million and are eligible to receive up to an additional $240.0 million in development and sales milestone payments from Pfizer. In addition, we are eligible to receive a tiered royalty on worldwide net sales of any potential products under the license at percentage royalty rates ranging from middle single-digits to low double-digits.

Research Projects

Our research projects leverage years of experience in developing lung-selective medicines to address the needs of patients suffering from respiratory illness. As a result of our strategic restructuring announced in September 2021, we intend to streamline and narrow our R&D focus on our highest value core respiratory opportunities. This would include the peak inspiratory flow rate ("PIFR") clinical study, in partnership with Viatris, to support the label update of YUPELRI and continued investment in our investigational inhaled Janus kinase inhibitor portfolio, with focus on the most advanced clinical candidate, nezulcitinib, initially targeting acute lung injury.

Our Strategy

Our core purpose is to create medicines that help improve the lives of patients suffering from respiratory illness. We strive to apply insight and innovation at each stage of our business, including research, development and commercialization. Our principle strategic objective is to leverage decades of respiratory expertise to discover and develop respiratory medicines that make a difference in people's lives.

We follow these core guiding principles in our mission to drive value creation:

- Focus on insight and innovation;
- Outsource non-core activities;
- Create and foster an integrated environment; and
- Aggressively manage uncertainty.

We manage our pipeline with the goal of optimizing program value and allocation of resources. We employ multiple strategies for commercialization of our products. Our approach may involve retaining product rights and marketing a product independently in the US or we may partner a product to extend our commercial reach, to expand our geographic reach, and/or to manage the financial risk associated with the program. Alternatively, we may monetize or divest an asset that we designate as outside our core business, where we believe the program is optimized by leveraging partner capabilities and removing or limiting our research and development costs.

Manufacturing

We rely primarily on a network of third-party manufacturers, including contract manufacturing organizations, to produce the active pharmaceutical ingredients ("API") and drug products required for our clinical trials and drug product. We believe that we and our partners have in-house expertise to manage this network of third-party manufacturers, and we believe that we will be able to continue to negotiate third-party manufacturing arrangements on commercially reasonable terms and that it will not be necessary for us to rely on internal manufacturing capacity in order to develop or, potentially, commercialize our products. However, if we are unable to obtain contract manufacturing or obtain such manufacturing on commercially reasonable terms, or if manufacturing is interrupted at one of our suppliers, whether due to regulatory or other reasons, we may not be able to develop our products or commercialize product as planned.

Any inability to acquire sufficient quantities of API or drug product in a timely manner from current or future sources could disrupt our research and development programs, the conduct of future clinical trials or our commercialization efforts. For more information, see the risk factor under the heading "*There is a single source of*

supply for a number of our product candidates and for YUPELRI, and our business will be harmed if any of these single-source manufacturers are not able to satisfy demand and alternative sources are not available" of this Annual Report on Form 10-K.

Government Regulation

The development and commercialization of pharmaceutical products and our product candidates by us, our collaboration partners and licensees, and those commercializing products in which we have an economic interest, such as GSK, and our ongoing research are subject to extensive regulation by governmental authorities in the US and other countries. Before marketing in the US, any medicine must undergo rigorous preclinical studies and clinical studies and an extensive regulatory approval process implemented by the FDA under the Federal Food, Drug, and Cosmetic Act. Outside the US, the ability to market a product depends upon receiving a marketing authorization from the appropriate regulatory authorities which are subject to equally rigorous regulatory obligations. The requirements governing the conduct of clinical studies, marketing authorization, pricing and reimbursement vary widely from country to country. In any country, however, the commercialization of pharmaceutical products is permitted only if the appropriate regulatory authority is satisfied that we have presented adequate evidence of the safety, quality and efficacy of the product.

Before commencing clinical studies in humans in the US, we must submit to the FDA an investigational new drug application ("IND") that includes, among other things, the general investigational plan and protocols for specific human studies and the results of preclinical studies. An IND will go into effect 30 days following its receipt by the FDA unless the FDA issues a clinical hold. Once clinical studies have begun under the IND, they are usually conducted in three phases and under FDA oversight. These phases generally include the following:

Phase 1. The product candidate is introduced into patients or healthy human volunteers and is tested for safety, dose tolerance and pharmacokinetics.

Phase 2. The product candidate is introduced into a limited patient population to assess the efficacy of the drug in specific, targeted indications, assess dosage tolerance and optimal dosage, and identify possible adverse effects and safety risks.

Phase 3. Phase 3 clinical trials are undertaken to further evaluate dosage, clinical efficacy, potency and safety in an expanded patient population at geographically dispersed clinical trial sites. These clinical trials are intended to establish the overall risk/benefit profile of the product and provide an adequate basis for product labeling.

The results of product development, preclinical studies and clinical studies must be submitted to the FDA as part of an NDA. The NDA also must contain extensive manufacturing information, and under the Pediatric Research Equity Act ("PREA"), certain applications for approval must also include an assessment, generally based on clinical study data, of the safety and effectiveness of the subject drug in relevant pediatric populations. The submission of an NDA generally requires payment of a substantial user fee to the FDA under the Prescription Drug User Fee Act ("PDUFA"), subject to certain limited deferrals, waivers and reductions. FDA's PDUFA performance goal is to review and act on 90 percent of priority new molecular entity ("NME") NDA submissions within 6 months of the 60-day filing date, and to review and act on 90 percent of standard NME NDA submissions within 10 months of the 60-day filing date. The FDA may determine that a Risk Evaluation and Management Strategy ("REMS") is necessary to ensure that the benefits of a product outweigh its risks. At the end of the review period, the FDA communicates either approval of the NDA or issues a complete response letter ("CRL") listing the application's deficiencies. The CRL may require additional testing or information, including additional pre-clinical or clinical data, for the FDA to reconsider the application. Even if such additional information and data are submitted, the FDA may decide that the NDA still does not meet the standards for approval. Data from clinical trials are not always conclusive and the FDA may interpret data differently than the sponsor. FDA approval of any application may include many delays or never be granted. If FDA grants approval, an approval letter authorizes commercial marketing of the product candidate with specific prescribing information for specific indications. Post-approval modifications to the drug, such as changes in indications, labeling, or manufacturing processes or facilities, may require a sponsor to develop additional data or conduct additional pre-clinical studies or clinical trials, to be submitted in a new or supplemental NDA, which would require FDA approval.

If an application is approved, drug products are subject to continuing regulation by the FDA, and the FDA may withdraw the product approval if compliance with post-marketing regulatory standards is not maintained or if safety or quality issues are identified after the product reaches the marketplace. In addition, the FDA may require post-marketing studies, sometimes referred to as Phase 4 studies, to monitor the safety and effectiveness of approved products, and may limit further marketing of the product based on the results of these post-marketing studies. The FDA has broad post-market regulatory and enforcement powers, including the ability to require changes to a product's approved labeling, including the addition of new warnings and contraindications, or the implementation of other risk management measures, including distribution-related restrictions, if there are new safety information developments, suspend or delay issuance of approvals, seize products, withdraw approvals, enjoin violations, and initiate criminal prosecution.

If regulatory approval for a medicine is obtained, the clearance to market the product will be limited to those diseases and conditions approved by FDA and for which the medicine was shown to be effective, as demonstrated through clinical studies and specified in the medicine's labeling. If this regulatory approval is obtained, a marketed medicine, its manufacturer and its manufacturing facilities are subject to continual review and periodic inspections by the FDA. The FDA ensures the quality of approved medicines, carefully monitoring manufacturers' compliance with its current Good Manufacturing Practice ("cGMP") regulations by conducting regular, periodic visits to re-inspect equipment, facilities, and processes following the initial approval of a product. Failure to comply with applicable cGMP requirements and conditions of product approval may lead the FDA to take enforcement actions or seek sanctions, including fines, issuance of warning letters, civil penalties, injunctions, suspension of manufacturing operations, operating restrictions, withdrawal of FDA approval, seizure or recall of products, and criminal prosecution. The cGMP regulations for drugs contain minimum requirements for the methods, facilities, and controls used in manufacturing, processing, and packaging of a medicine. The regulations are intended to make sure that a medicine is safe for use, and that it has the ingredients and strength it claims to have. Discovery of previously unknown problems with a medicine, manufacturer or facility may result in restrictions on the medicine or manufacturer, including fines, issuance of warning letters, civil penalties, injunctions, suspension of manufacturing operations, operating restrictions, costly recalls, withdrawal of FDA approval, and criminal prosecution.

Additionally, the FDA and other federal regulatory agencies closely regulate the marketing and promotion of drugs through, among other things, standards and regulations for direct-to-consumer advertising, advertising and promotion to healthcare professionals, communications regarding unapproved uses, industry-sponsored scientific and educational activities, and promotional activities involving the Internet. A product cannot be promoted before it is approved. After approval, product promotion can include only those claims relating to safety and effectiveness that are consistent with the labeling approved by the FDA. Healthcare providers are permitted to prescribe drugs for "off-label" uses - that is, uses not approved by the FDA and not described in the product's labeling - because the FDA does not regulate the practice of medicine. However, FDA regulations impose restrictions on manufacturers' communications regarding off-label uses. Broadly speaking, a manufacturer may not promote a drug for off-label use, but under certain conditions may engage in non-promotional, balanced, scientific communication regarding off-label use. Failure to comply with applicable FDA requirements and restrictions in this area may subject a company to adverse publicity and enforcement action by the FDA, the Department of Justice, or the Office of the Inspector General of the Department of Health and Human Services, as well as state authorities. This could subject a company to a range of penalties that could have a significant commercial impact, including civil and criminal fines and agreements that materially restrict the manner in which a company promotes or distributes a drug.

We, our collaboration partners and licensees are also subject to various laws and regulations regarding laboratory practices, the experimental use of animals and the use and disposal of hazardous or potentially hazardous substances in connection with our research. In each of these areas, as above, the FDA and other regulatory authorities have broad regulatory and enforcement powers, including the ability to suspend or delay issuance of approvals, seize products, withdraw approvals, enjoin violations, and initiate criminal prosecution, any one or more of which could have a material adverse effect upon our business, financial condition and results of operations.

Outside the US, the ability to market products will also depend on receiving marketing authorizations from the appropriate regulatory authorities. Risks similar to those associated with FDA approval described above exist with the regulatory approval processes in other countries.

United States Healthcare Reform

The Patient Protection and Affordable Care Act, as amended (the "Healthcare Reform Act"), substantially changed the way healthcare is financed by both governmental and private insurers, and impacts pricing and reimbursement of YUPELRI and the marketed drugs with respect to which we are entitled to royalty or similar payments, and related commercial operations. Certain provisions of the Healthcare Reform Act have been subject to judicial challenges as well as efforts to modify them or to alter their interpretation or implementation. We expect that the Healthcare Reform Act, its implementation, efforts to modify, or invalidate, the Healthcare Reform Act or portions thereof, or its implementation, and other healthcare reform measures that may be adopted in the future, could have a material adverse effect on our industry generally and on the ability of us, our collaboration partners, or those commercializing products with respect to which we have an economic interest or right to receive royalties to maintain or increase sales of our existing products or to successfully commercialize our product candidates, if approved. For more information, see the risk factor under the heading *"Changes in healthcare law and implementing regulations, including government restrictions on pricing and reimbursement, as well as healthcare policy and other healthcare payor cost-containment initiatives, may negatively impact us, our collaboration partners, or those commercializing products with respect to which we have an economic interest or right to receive royalties"* of this Annual Report on Form 10-K.

Pharmaceutical Pricing and Reimbursement

We participated in and had certain price reporting obligations under the Medicaid Drug Rebate and other programs for VIBATIV ® for which we remain responsible, as described in greater detail under the risk factor *"If we failed to comply with our reporting and payment obligations under the Medicaid Drug Rebate program or other governmental pricing programs, we could be subject to additional reimbursement requirements, penalties, sanctions and fines, which could have a material adverse effect on our business, financial condition, results of operations and growth prospects"* of this Annual Report on Form 10-K.

Our ability, and the ability of our collaboration partners, licensees, or those commercializing products with respect to which we have an economic interest or right to receive royalties to commercialize our products successfully, and our ability to attract commercialization partners for our products, depends in significant part on the availability of adequate financial coverage and reimbursement from third-party payors, including, in the US, governmental payors such as the Medicare and Medicaid programs, managed care organizations, and private health insurers. The reimbursement environment is described in greater detail under the risk factor *"Changes in healthcare law and implementing regulations, including government restrictions on pricing and reimbursement, as well as healthcare policy and other healthcare payor cost-containment initiatives, may negatively impact us, our collaboration partners, or those commercializing products with respect to which we have an economic interest or right to receive royalties"* of this Annual Report on Form 10-K.

Fraud and Abuse Laws

Our interactions and arrangements with customers and third-party payors are subject to applicable US federal and state fraud and abuse laws and equivalent third country laws. These laws and the related risks are described in greater detail under the risk factor "*Our relationships with customers and third-party payors are subject to applicable anti-kickback, fraud and abuse, transparency and other healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties, exclusion, contractual damages, reputational harm and diminished profits and future earnings*" of this Annual Report on Form 10-K.

Data Privacy and Protection

We are subject to laws and regulations that address privacy and data security. In the US, numerous federal and state laws and regulations, including state data breach notification laws, state health information and/or genetic privacy laws, and federal and state consumer protection laws (e.g., Section 5 of the Federal Trade Commission Act ("FTC Act")), govern the collection, use, disclosure, and protection of health-related and other personal information. Similar obligations apply outside of the US. For example, the General Data Protection Regulation ("GDPR") which entered into force on May 25, 2018 amplified existing data protection obligations in the EU. These laws and related risks are described in greater detail under the risk factor *"If we fail to comply with data protection laws and regulations, we could be subject to government enforcement actions (which could include civil or criminal penalties), private litigation and/or*

adverse publicity, which could negatively affect our operating results and business" of this Annual Report on Form 10-K.

Patents and Proprietary Rights

We will be able to protect our technology from unauthorized use by third parties only to the extent that our technology is covered by valid and enforceable patents or is effectively maintained as trade secrets. Our success in the future will depend in part on obtaining patent protection for our product candidates. Accordingly, patents and other proprietary rights are essential elements of our business. Our policy is to seek in the US and selected foreign countries patent protection for novel technologies and compositions of matter that are commercially important to the development of our business. For proprietary know-how that is not patentable, processes for which patents are difficult to enforce and any other elements of our drug discovery process that involve proprietary know-how and technology that is not covered by patent applications, we rely on trade secret protection and confidentiality agreements to protect our interests. We require all of our employees, consultants and advisors to enter into confidentiality agreements. Where it is necessary to share our proprietary information or data with outside parties, our policy is to make available only that information and data required to accomplish the desired purpose and only pursuant to a duty of confidentiality on the part of those parties.

As of December 31, 2021, we owned 285 issued US patents and 1,968 granted foreign patents, as well as additional pending US patent applications and foreign patent applications. The claims in these various patents and patent applications are typically directed to compositions of matter, including claims covering product candidates, crystalline forms, lead compounds and key intermediates, pharmaceutical compositions, methods of use and/or processes for making our compounds. In particular, our wholly-owned subsidiary Theravance Biopharma R&D IP, LLC owns the following US patents which are listed in the FDA *Approved Drug Products with Therapeutic Equivalence Evaluations* (Orange Book) for YUPELRI (revefenacin) inhalation solution: US Patent No. 7,288,657, expiring on December 23, 2025; US Patent No. 7,491,736, expiring March 10, 2025; US Patent No. 7,521,041, expiring March 10, 2025; US Patent No. 7,550,595, expiring March 10, 2025; US Patent No. 7,585,879, expiring March 10, 2025; US Patent No. 7,910,608, expiring March 10, 2025; US Patent No. 8,034,946, expiring March 10, 2025; US Patent No. 8,053,448, expiring March 10, 2025; US Patent No. 8,273,894, expiring March 10, 2025; US Patent No. 8,541,451, expiring August 25, 2031; US Patent No. 9,765,028, expiring July 14, 2030; US Patent No. 10,106,503, expiring March 10, 2025; US Patent No. 10,343,995, expiring March 10, 2025; US Patent No. 10,550,081, expiring July 14, 2030; and US Patent No. 11,008,289, expiring July 14, 2030 (each of the aforementioned expiration dates not including any patent term extensions that may be available under the Drug Price Competition and Patent Term Restoration Act of 1984). Thus, the last to expire patent currently listed in the Orange Book for YUPELRI (revefenacin) inhalation solution expires on August 25, 2031. On December 19, 2018, we filed patent term extension ("PTE") applications in the US Patent and Trademark Office ("USPTO") for US Patent Nos. 7,288,657 and 7,585,879. These PTE applications are currently pending and if granted, we will be permitted to extend the term of one of these patents for the period determined by the USPTO.

Issued US and foreign patents generally expire 20 years after their filing date. The patent rights relating to YUPELRI (revefenacin) inhalation solution currently consist of issued US patents, pending US patent applications and counterpart patents and patent applications in a number of jurisdictions, including Europe. Additionally, our patent rights relating to nezulcitinib currently include an issued US composition of matter patent that expires in 2039 (not including any patent term extensions that may be available under the Drug Price Competition and Patent Term Restoration Act of 1984), as well as additional pending patent applications in a number of jurisdictions. Nevertheless, issued patents can be challenged, narrowed, invalidated or circumvented, which could limit our ability to stop competitors from marketing similar products and threaten our ability to commercialize our product candidates. Our patent position, similar to other companies in our industry, is generally uncertain and involves complex legal and factual questions. To maintain our proprietary position, we will need to obtain effective claims and enforce these claims once granted. It is possible that, before any of our products can be commercialized, any related patent may expire or remain in force only for a short period following commercialization, thereby reducing any advantage of the patent. Also, we do not know whether any of our patent applications will result in any issued patents or, if issued, whether the scope of the issued claims will be sufficient to protect our proprietary position.

Patent Term Restoration and Regulatory Exclusivities

Depending upon the timing, duration, and specifics of FDA approval of our product candidates, some of our United States patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, referred to as the Hatch-Waxman Act. The Hatch-Waxman Act permits a patent restoration term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. However, patent term restoration cannot extend the remaining term of a patent beyond a total of 14 years from the product's approval date. The patent term restoration period is generally one-half the time between the effective date of an IND, and the submission date of an NDA, plus the time between the submission date of an NDA and the approval of that application, except that the period is reduced by any time during which the applicant failed to exercise due diligence. Only one patent applicable to an approved drug is eligible for the extension, and the extension must be applied for prior to expiration of the patent and within 60 days of approval. The United States Patent and Trademark Office, in consultation with the FDA, reviews and approves the application for any patent term extension or restoration.

The Hatch-Waxman Act also provides periods of regulatory exclusivity for products that would serve as a reference listed drug, or RLD, for an abbreviated new drug application, or ANDA, or application submitted under section 505(b)(2) of the FDCA, or 505(b)(2) application. If a product is a new chemical entity, or NCE — generally meaning that the active moiety has never before been approved in any drug — there is a period of five years from the product's approval during which the FDA may not accept for filing any ANDA or 505(b)(2) application for a drug with the same active moiety. An ANDA or 505(b)(2) application may be submitted after four years, however, if the sponsor of the application makes a "Paragraph IV" certification.

A may also qualify for a three-year period of exclusivity if the NDA contains new clinical data (other than bioavailability studies), derived from studies conducted by or for the sponsor, that were necessary for approval. In that instance, the exclusivity period does not preclude filing or review of an ANDA or 505(b)(2) application; rather, the FDA is precluded from granting final approval to the ANDA or 505(b)(2) application until three years after approval of the RLD. Additionally, the exclusivity applies only to the conditions of approval that required submission of the clinical data.

Once the FDA accepts for filing an ANDA or 505(b)(2) application containing a Paragraph IV certification, the applicant must within 20 days provide notice to the RLD NDA holder and patent owner that the application has been submitted and provide the factual and legal basis for the applicant's assertion that the patent is invalid or not infringed. If the NDA holder or patent owner files suit against the ANDA or 505(b)(2) applicant for patent infringement within 45 days of receiving the Paragraph IV notice, the FDA is prohibited from approving the ANDA or 505(b)(2) application for a period of 30 months or the resolution of the underlying suit, whichever is earlier. If the RLD has NCE exclusivity and the notice is given and suit filed during the fifth year of exclusivity, the regulatory stay extends until 7.5 years after the RLD approval. The FDA may approve the proposed product before the expiration of the regulatory stay if a court finds the patent invalid or not infringed or if the court shortens the period because the parties have failed to cooperate in expediting the litigation.

Competition

Our core development programs, and the marketed products to which we are entitled to profit share revenue, royalty or similar payments is focused on respiratory therapeutics. Our commercial infrastructure is focused primarily on the acute care setting. We expect that any respiratory medicines that we commercialize with our collaborative partners or on our own will compete with existing and future market-leading medicines.

Many of our competitors have substantially greater financial, technical and personnel resources than we have. In addition, many of these competitors have significantly greater commercial infrastructures than we have. Our ability to compete successfully will depend largely on our ability to leverage our experience in drug discovery, development and commercialization to:

- discover and develop respiratory medicines that are superior to other products in the market;
- attract and retain qualified scientific, clinical development and commercial personnel;

- obtain patent and/or other proprietary protection for our medicines and technologies;
- obtain required regulatory approvals;
- commercialize approved products; and
- successfully collaborate with pharmaceutical companies in the discovery, development and commercialization of new respiratory medicines.

YUPELRI (revefenacin) inhalation solution, a long-acting muscarinic antagonist (LAMA)

YUPELRI competes predominately with the nebulized LAMA Lonhala® Magnair® (glycopyrrolate) dosed two times per day and with short acting nebulized bronchodilators that are dosed three to four times per day.

TRELEGY or FF/UMEC/VI (fluticasone furoate/umeclidinium bromide/vilanterol)

For treatment of COPD, TRELEGY competes in all major markets with AstraZeneca's Breztri® Aerosphere® (budesonide/glycopyrronium/formoterol fumarate, dosed twice per day). Trimbow (beclometasone dipropionate/formoterol fumarate/glycopyrronium bromide, dosed twice per day) from Chiesi Farmaceutici is an additional COPD competitor in Europe.

For treatment of asthma, TRELEGY is the only triple therapy approved in the US and competes in Japan with Novartis's Enerzair® Breezhaler® (indacaterol acetate, glycopyrronium bromide and mometasone furoate, dosed once daily).

In both COPD and asthma, TRELEGY also competes with "open triple" therapy which can be accomplished by the concurrent use of two or three products. An example of such use includes a LABA/ICS combination such as AstraZeneca's Symbicort and a LAMA such as Boehringer Ingelheim's Spiriva.

Human Capital

Workforce Demographics

As of December 31, 2021, we had 159 employees, 158 full-time and one part-time. Of these employees, 143 were in the US, and 16 were non-US. As previously disclosed, due to the Restructuring event in September 2021, approximately 75% of our headcount was reduced, with approximately 75% of the reduction taking place in November 2021 and the remainder to be completed in February 2022, leaving approximately 106 employees as part of the new structure.

Culture and Employee Engagement

We consider our employee relations first-rate and strive to provide a culture of purpose, engagement, and learning. Theravance has a strong value proposition anchored in our Core Values—*We Think it Through*, *We Find a Way*, *We Get it Done*, and *We Win Together.* We strive to live these values across the Company every day, integrating them into everything from our interview, hiring, and onboarding processes to our *PULSE* performance process, total rewards, and recognition programs. In addition to valuing professional qualifications, we emphasize the importance of character and integrity, fostering a culture of empowerment where employees have ownership in business outcomes. Reflected in our Core Values are behaviors that keep our people engaged and working collaboratively. Our employees are encouraged to ask questions, make suggestions, and provide input through many forms of corporate communication such as an open-door policy, all-employee meetings, an anonymous online suggestion box, and an employee *PULSE* survey.

Our employee *PULSE* survey is designed to assist us in measuring overall employee engagement and consistently achieves participation rates between 85-92%. 2021 survey scores averaged in the positive range from 4.1 to 4.6 on a scale of 1 (Strongly Disagree) through 5 (Strongly Agree). Our highest score on average (4.6) was related to the frequency of discussions with managers. When compared to October 2020, there was a significant increase in the frequency of discussions with managers (from 3.9 to 4.6) and a slight increase in senior leadership communication (from

3.9 to 4.3). These survey results provide important insight into organizational success and opportunity, allowing potential variation in overall satisfaction to be identified and addressed as we move forward.

We have significant retention incentives in place post-Restructuring. These include a special incentive compensation program of both long- and short-term offerings and an engagement plan that connects the importance of achieving our core purpose to the strength of our connections and team-building. In addition, through *Reimagining Theravance*, we empowered and engaged employees to provide feedback on our existing operating model and actively set the foundation for a hybrid-remote operating model to be launched in 2022. Our reimagined operating model celebrates the increased flexibility and productivity many employees reported during remote work while allowing broad access to office workstations and the in-person collaborations that elevate our culture and give us our competitive advantage.

We expect all employees to observe the highest levels of business ethics while delivering the highest levels of performance. These expectations are outlined and reinforced in various documents and forms of communication within and across our Company. The Company encourages employees to speak up and raise questions and concerns promptly about any situation that may violate our Code of Business Conduct, our Core Values, or our policies. We believe that it benefits the entire Company for employees to raise concerns so the Company may consider them carefully and address them appropriately. We seek to promote an environment that fosters honest communications about matters of conduct related to our business activities, whether that conduct occurs within the Company, involves one of the Company's contractors, suppliers, consultants, clients, or any other party with a business relationship with the Company. We work diligently to make clear that management is prepared to address any reported violations and ensure that it is known that any form of retaliation is strictly prohibited. In addition, we have an easily accessible hotline available to employees wishing to report complaints anonymously.

Diversity, Equity, and Inclusion

As an equal opportunity employer, we strive to build and maintain a culture of diversity, equity, and inclusion through both our business and human resources practices and policies. We work to eliminate discrimination and harassment in all its forms, including related to color, race, sex or gender, sexual orientation, gender identity, age, pregnancy, caste, disability, ethnicity, national origin, ancestry, religious beliefs, veteran status, uniformed service member status, or physical or mental disability. We strive to build and foster a culture where all employees feel empowered to be their authentic selves. Our Diversity, Equity & Inclusion Council and Women's Leadership Network are Company-sponsored, employee-led groups that aim to improve attraction, retention, development, inclusion, and engagement of a diverse and global workforce. For the benefit of our employees, patients, and community, we must celebrate, encourage, and support similarities and differences to drive innovation.

Talent, Development, and Total Rewards

We believe that our talent strategy of providing exciting career growth and development opportunities, recognizing and rewarding performance, providing competitive compensation and benefits assists us in attracting and retaining the best talent. We believe we are successful in our retention efforts because we provide challenging work assignments, cross-functional teamwork experiences, and career progression supported by new skill-building. We invest in employee learning and development by identifying and providing training and development programs, speakers, tuition reimbursement, and cross-training in areas of interest beyond hired role. We strive to average between 25-35 training hours per employee per year.

We offer a competitive total rewards package that supports our business strategy to attract, retain and reward our employees in a highly competitive market. Our employees are provided with a strong base salary, cash bonus opportunities, equity incentives, health and wellness benefits, and programs. We regularly evaluate our compensation programs with an independent consultant and utilize industry benchmarking. In addition, we provide a variety of programs and services that meet our employees' needs and encourage work-life balance. These services include competitive and affordable healthcare and additional insurance benefits for both full-time and part-time employees, including eligible dependents. We also match contributions to tax-qualified defined contribution savings (401k) plans, offer an employee share purchasing plan ("ESPP"), and provide training and development programs designed to improve workplace performance while supporting flexible, hybrid-remote working.

Understanding the importance of goal setting and ongoing career development conversations, Theravance Biopharma requires managers and employees to play an active role in the *PULSE* performance management process at monthly, quarterly, and annual frequencies. *PULSE* is designed to increase clarity and accountability for roles and responsibilities, strengthen communication, build trust, all while championing personal and professional growth, learning, and success.

Great teamwork is a critical foundation for Theravance Biopharma. The *TheraStars Rewards and Recognition Program* helps us maintain a culture of recognition and teamwork by offering various options for our employees and managers to recognize and reward colleagues across the organization. In 2021, 97% of our employee population were active registered users, with each user averaging seven awards sent in recognition. These moments of celebration establish, reinforce, and maintain our sense of community and teamwork so critical in our ability to achieve our core purpose.

Workplace Safety and COVID-19

Workplace safety is always a priority for Theravance Biopharma. To maintain a safe and healthy workplace, we have implemented initiatives, procedures, and policies designed to address risk and stay compliant with relevant national and international health and safety standards.

In response to COVID-19, our COVID Task Force continues to lead the Company through the evolution of a pandemic with a continued focus on employee wellness and safety, policy updates based on Centers for Disease Control and Prevention ("CDC"), county, federal and state guidelines, and ongoing employee communication. As part of this evolution, we have an initiative in place to move to a strategically flexible workforce, encouraging a hybrid-remote model, allowing us to reimagine how we work, and propelling us to emerge as a stronger, more nimble company.

Financial Information About Geographic Areas

Information on our total revenues attributed to geographic areas and customers who represented at least 10% of our total revenues is included in "*Item 8, Note 4. Segment Information,*" to our consolidated financial statements in this Annual Report on Form 10-K.

Corporation Information

Theravance Biopharma was incorporated in the Cayman Islands in July 2013 under the name Theravance Biopharma, Inc. Theravance Biopharma began operating as an independent, publicly-traded company on June 2, 2014 following a spin-off from Innoviva, Inc. Our corporate address in the Cayman Islands and principal executive office is P.O. Box 309, Ugland House, Grand Cayman, KY1-1104, Cayman Islands and the address of our wholly-owned US operating subsidiary Theravance Biopharma US, Inc. is 901 Gateway Boulevard, South San Francisco, California 94080. While Theravance Biopharma is incorporated under Cayman Island law, the Company became an Irish tax resident effective July 1, 2015. The address of our wholly-owned Irish operating subsidiary, Theravance Biopharma Ireland Limited, is Connaught House, Burlington Road, Dublin 4, Ireland.

Available Information

Our Internet address is *www.theravance.com*. Our investor relations website is located at *https://investor.theravance.com*. We make available free of charge on our investor relations website under "SEC Filings" our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K, our directors' and officers' Section 16 Reports and any amendments to those reports as soon as reasonably practicable after filing or furnishing such materials to the US Securities and Exchange Commission ("SEC"). Our current Code of Business Conduct, Corporate Governance Guidelines, Articles of Association, Board of Director Committee Charters, and other materials, including amendments thereto, may also be found on our investor relations website under "Corporate Governance." The information found on our website is not part of this or any other report that we file with or furnish to the SEC. Theravance Biopharma and the Theravance Biopharma logo are registered trademarks of the Theravance Biopharma group of companies. Trademarks, tradenames or service marks of other companies appearing in this report are the property of their respective owners.

ITEM 1A. RISK FACTORS

The risks described below and elsewhere in this Annual Report on Form 10-K and in our other public filings with the SEC are not the only risks facing the Company. Additional risks and uncertainties not currently known to us or that we currently deem to be not material also may materially adversely affect our business, financial condition and/or operating results.

Summary of Principal Risks Associated with Theravance Biopharma's Business

- We anticipate that we may incur losses for the foreseeable future on a US GAAP basis. We may never achieve or sustain profitability;
- We face risks related to health epidemics, including the recent COVID-19 pandemic, which could have a material adverse effect on our business and results of operations;
- We do not control TRC and, in particular, have no control over the GSK Partnered Respiratory Programs, including TRELEGY, or access to non-public information regarding the development of the GSK Partnered Respiratory Programs;
- If there are any adverse developments or perceived adverse developments with respect to the GSK-Partnered Respiratory Programs in which we have a substantial economic interest, including TRELEGY, our business will be harmed, and the price of our securities could fall;
- Any delay in commencing or completing clinical studies for product candidates and any adverse results from clinical or non-clinical studies or regulatory obstacles product candidates may face, would harm our business and the price of our securities could fall;
- If our product candidates are not approved by regulatory authorities, including the FDA, we will be unable to commercialize them;
- If sufficient capital is not available, we may have to further curtail operations or we could be forced to share our rights to commercialize our product candidates with third parties on terms that may not be favorable to us;
- We may fail to achieve the expected cost savings and related benefits from our September 2021 Restructuring;
- If our partners do not satisfy their obligations under our agreements with them, or if they terminate our partnerships with them, we may not be able to develop or commercialize our partnered product candidates as planned; and
- Our ongoing drug discovery and development efforts might not generate additional successful product candidates or approvable drugs.

RISKS RELATING TO THE COMPANY

We anticipate that we will incur losses for the foreseeable future. We may never achieve or sustain profitability.

First as part of Innoviva, Inc., and since June 2, 2014 as Theravance Biopharma, we have been engaged in discovery and development of compounds and product candidates since mid-1997. We may never generate sufficient revenue from the sale of medicines, royalties on sales by our partners or from our interest in Theravance Respiratory Company, LLC ("TRC") to achieve profitability. During the years ended December 31, 2021, 2020, and 2019, we recognized net losses of $199.4 million, $278.0 million and $236.5 million, respectively, which are reflected in the

shareholders' deficit on our consolidated balance sheets. We reflect cumulative net loss incurred after June 2, 2014, the effective date of our spin-off from Innoviva, Inc. (the "Spin-Off"), as accumulated deficit on our consolidated balance sheets, which was $1.7 billion as of December 31, 2021. We expect to continue to incur net losses at least over the next several years as we continue our drug discovery and development efforts and incur preclinical and clinical development costs related to our current product candidates and commercialization and development costs relating to YUPELRI. In particular, to the extent we continue to advance our product candidates into and through additional clinical studies, we will incur substantial expenses. For example, we initiated a Phase 2b/3 induction and maintenance study of izencitinib in ulcerative colitis, we initiated a Phase 2 induction study of izencitinib in Crohn's disease, and we have progressed ampreloxetine (TD-9855) into a Phase 3 registrational program. The expenses associated with these clinical studies are substantial and, as there was the unfavorable outcome in two of the studies, the compounds are unlikely to generate substantial revenues. While our YUPELRI operations were profitable on a brand basis for the second half of 2020, we will continue to incur costs and expenses associated with the commercialization of YUPELRI in the United States ("US"), including the maintenance of an independent sales and marketing organization with appropriate technical expertise, a medical affairs presence and consultant support, and post-marketing studies. Our commitment of resources to the continued development of our existing product candidates, our discovery programs, and YUPELRI will require significant additional funding. Our operating expenses also will increase if, among other things:

- our earlier stage potential products move into later-stage clinical development, which is generally more expensive than early stage development;
- additional preclinical product candidates are selected for clinical development;
- we pursue clinical development of our potential or current products in new indications;
- our clinical trials become more complicated due to the COVID-19 pandemic or other external factors;
- we increase the number of patents we are prosecuting or otherwise expend additional resources on patent prosecution or defense; or
- we acquire or in-license additional technologies, product candidates, products or businesses.

While we are generating revenues and income from (i) sales of YUPELRI, (ii) our economic interest in royalties from net sales of TRELEGY paid to TRC (63.75% of which amounts are used to make payments on the Non-Recourse 2035 Notes), (iii) payments under collaboration agreements, and (iv) minor royalties from the net sales of VIBATIV, we do not expect to generate significant revenues or become profitable in the near future. As a result of the COVID-19 pandemic (defined below), we could experience declines in revenues from these sources. If we or our collaborators or licensees are not able to successfully develop additional products, obtain required regulatory approvals, manufacture products at an acceptable cost or with appropriate quality, or successfully market and sell such products with desired margins, our expenses will continue to exceed any revenues we may receive for the foreseeable future.

In the absence of substantial licensing payments, contingent payments or other revenues from third-party collaborators, royalties on sales of products licensed under our intellectual property rights, or other sources of revenues, we will continue to incur operating losses and will require additional capital to execute our business strategy. The likelihood of reaching, and the time required to reach, and then to sustain, profitability are highly uncertain. As a result, we expect to continue to incur substantial losses for the foreseeable future. We are uncertain when or if we will ever be able to achieve or sustain profitability. Failure to become and remain profitable would adversely affect the price of our securities and our ability to raise capital and continue operations.

We face risks related to health epidemics, including the recent COVID-19 pandemic, which could have a material adverse effect on our business and results of operations.

Our business has been and will continue to be adversely affected by the recent widespread and contagious outbreak of respiratory illness caused by a novel strain of coronavirus, SARS-CoV-2, causing the Coronavirus Disease 2019, also known as COVID-19 (the "COVID-19 pandemic"). Global health concerns relating to the COVID-19 pandemic have weighed on the macroeconomic environment, and the pandemic has significantly increased economic volatility and uncertainty.

The pandemic resulted in government authorities implementing numerous measures to try to contain the virus, such as travel bans and restrictions, quarantines, shelter-in-place or stay-at-home orders, and business shutdowns. These measures have adversely impacted and may further impact our employees and operations and the operations of our customers, suppliers and business partners, and may negatively impact spending patterns, payment cycles and insurance coverage levels. In addition, certain aspects of our business, such as laboratory-based research, cannot be conducted remotely and other aspects of our business, like our hospital-based sales team, our field-based medical affairs team, and our support of sites in our clinical trials, cannot be accomplished as effectively or efficiently remotely. These measures by government authorities, as well as the precautions we will take in order to operate our business responsibly in light of the COVID-19 pandemic, may continue to remain in place for a significant period of time, and they are likely to continue to adversely affect our business and results of operations.

In addition, we expect sales cycles, particularly for new customers, to continue to be impacted as a result of the COVID-19 pandemic, and we have observed continued volatility in YUPELRI sales. Sales momentum has been affected by COVID-19 and may continue to be in the future. We market YUPELRI in the hospital setting, where healthcare workers are prioritizing the treatment of patients with or suspected of COVID-19 disease and to pulmonologists, whose practices have been impacted by the pandemic. In mid-March 2020, we suspended in-person sales calls to accounts in response to the COVID-19 pandemic. In August 2020, we began reengaging with these customers in-person when certain criteria are met and remotely via telephone calls, electronic mail, digital outreach or video conferencing as we seek to continue to support healthcare professionals and patient care. We are now able to more frequently conduct in-person customer engagements, however there is still high variability of access regionally. Customer orders or new patient use of YUPELRI may decline as a result of, among other things, a shift in our marketing efforts, increased workload of healthcare providers, and the impact of the Center for Disease Control interim guidelines for limiting the exposure of health care workers to the virus that causes COVID-19, in which drug nebulization in COVID-19 positive patients is listed as a high-risk procedure while present in the room for procedures when the healthcare providers' eyes, nose, or mouth are not protected. We are preparing for continued volatility as disruptions of day-to-day operations of hospitals and clinics may continue. In addition, while we do not currently anticipate any supply issues, the COVID-19 pandemic could impact our supply of YUPELRI in the future. At this stage, we are unable to predict with certainty the ultimate disruptive impact of the COVID-19 pandemic on both YUPELRI and the rest of our business.

In addition, the COVID-19 pandemic makes the conduct of clinical trials more challenging given the paramount importance of adequate safety monitoring, collection of data and distribution of study drug, all of which are traditionally achieved by in-person visits to our study sites. Challenges may continue to arise from quarantines, shelter-in-place or stay-at-home orders, site closures, travel limitations, potential interruptions to the supply chain for investigational products, other measures to help prevent the spread of COVID-19 or other considerations if site personnel or trial participants become infected with COVID-19. These challenges may lead to difficulties in meeting protocol-specified procedures. In light of the COVID-19 pandemic, the Company implemented mitigation plans to help ensure patients in the clinical trials have continued access to drug supply and regular visits with their physicians for study visits per trial protocols, but there is a risk that our trial data could be impacted if our efforts are insufficient. It is also possible that demand for products that we may pursue could be materially and adversely affected as a result of COVID-19 and any related economic impact. Furthermore, we cannot assure you that our publicly-announced initiatives addressing COVID-19 will result in commercially-viable products.

The spread of COVID-19 has caused us to modify our business practices and we may take further actions as may be required by government authorities or that we determine are in the best interests of our employees, customers and business partners. There is no certainty that such actions will be sufficient to mitigate the risks posed by the virus or otherwise be satisfactory to government authorities. If significant portions of our workforce, and particularly our field-

based teams and laboratory staff, are unable to work effectively, including due to illness, quarantines, social distancing, government actions or other restrictions in connection with the COVID-19 pandemic, our operations will be impacted. The COVID-19 pandemic could limit the ability of our customers, suppliers and business partners to perform under their contracts with us, including third-party payers' ability to make timely payments to us during and following the pandemic. We may also experience a shortage of supplies and materials or a suspension of services from third parties. Additionally, while the potential economic impact brought by, and the duration of, the coronavirus pandemic is difficult to assess or predict, the impact of the coronavirus on the global financial markets may reduce our ability to access capital, which could negatively impact our long-term liquidity. Even after the COVID-19 pandemic subsides, we may continue to experience an adverse impact to our business as a result of its global economic impact.

The extent to which the COVID-19 pandemic impacts our business, results of operations and financial condition will depend on future developments, which are highly uncertain and difficult to predict, including, but not limited to, the duration and spread of the pandemic, its severity, the actions to contain the virus or address its impact, vaccine rollout, distribution and acceptance, and how quickly and to what extent normal economic and operating activities can resume. There are no comparable recent events which may provide guidance as to the effect of the spread of the COVID-19 pandemic, and, as a result, the ultimate impact of the COVID-19 pandemic or a similar health epidemic is highly uncertain and subject to change. We do not yet know the full extent of COVID-19's impact on our business, our operations, or the global economy as a whole. However, the effects are likely to continue to have a material adverse impact on our future results of operations.

We do not control TRC and, in particular, have no control over the GSK-Partnered Respiratory Programs or access to non-public information regarding the development of the GSK-Partnered Respiratory Programs.

Innoviva assigned to TRC its strategic alliance agreement with GSK and all of its rights and obligations under its LABA collaboration agreement other than with respect to RELVAR ELLIPTA/BREO ELLIPTA, ANORO ELLIPTA and vilanterol monotherapy. Our equity interest in TRC entitles us to an 85% economic interest in any future payments made by GSK under the strategic alliance agreement and under the portion of the collaboration agreement assigned to TRC (the "GSK Agreements") (net of TRC expenses paid and the amount of cash, if any, expected to be used by TRC pursuant to the TRC LLC Agreement over the next four fiscal quarters), which agreements govern Innoviva's and GSK's respective interests in the GSK-Partnered Respiratory Programs. Our equity interest primarily covers TRELEGY (the combination of fluticasone furoate, umeclidinium, and vilanterol in a single ELLIPTA inhaler) products. Our economic interest does not include any payments by GSK associated with RELVAR ELLIPTA/BREO ELLIPTA, ANORO ELLIPTA or vilanterol monotherapy. Innoviva controls TRC and, except for certain consent rights, we have no right to participate in the business and affairs of TRC. Innoviva has the exclusive right to appoint TRC's manager who, among other things, is responsible for the day-to-day management of the GSK-Partnered Respiratory Programs and exercises the rights relating to the GSK-Partnered Respiratory Programs. As a result, we have no rights to participate in, or access to non-public information about, the development and commercialization work GSK and Innoviva are undertaking with respect to the GSK-Partnered Respiratory Programs and no right to enforce rights under the GSK Agreements assigned to TRC. We have had and may in the future have disagreements with Innoviva and TRC regarding Innoviva's decisions regarding the management of TRC. The dispute resolution procedures set forth in the TRC LLC Agreement have been invoked two times to date. These procedures can divert management's attention and require us to incur significant costs. Further, if resolved in a manner adverse to our interests, these procedures and the actions that lead to them could have a material impact on our operations. See the Risk Factor entitled "*We do not control the commercialization of TRELEGY and we do not control TRC; accordingly the amount of royalties we receive will depend on, among other factors, GSK's ability to further commercialize TRELEGY and TRC's decisions concerning use of cash in accordance with the TRC LLC Agreement*" for more information. Moreover, we have many of the same risks with respect to our and TRC's dependence on GSK as we have with respect to our dependence on our own partners, including any adverse impacts on GSK's operations as a result of the COVID-19 pandemic.

If there are any adverse developments or perceived adverse developments with respect to the GSK-Partnered Respiratory Programs in which we have a substantial economic interest, including TRELEGY, our business will be harmed, and the price of our securities could fall.

We have no access to non-public information regarding the development progress of, or plans for, the GSK-Partnered Respiratory Programs, including TRELEGY, and we have little, if any, ability to influence the progress of those programs because our interest in these programs is only through our ownership interest in TRC, which is

controlled by Innoviva. However, if any of the GSK-Partnered Respiratory Programs in which we have a substantial economic interest encounter delays, do not demonstrate required quality, safety and efficacy, are terminated, or if there are any adverse developments or perceived adverse developments with respect to such programs, our business will be harmed, and the price of our securities could fall. Examples of such adverse developments include, but are not limited to:

- disappointing or lower than expected sales of TRELEGY;
- the emergence of new closed triple or other alternative therapies or any developments regarding competitive therapies, including comparative price or efficacy of competitive therapies;
- disputes between GSK and Innoviva or between us and Innoviva, such as our 2019 arbitration and the arbitration with Innoviva that was completed in early 2021 (see *"Risk Factors—We do not control the commercialization of TRELEGY and we do not control TRC; accordingly the amount of royalties we receive will depend on, among other factors, GSK's ability to further commercialize TRELEGY and TRC's decisions concerning use of cash in accordance with the TRC LLC Agreement"*);
- GSK deciding to modify, delay or halt the TRELEGY program;
- the FDA and/or other national or foreign regulatory authorities determining that any of the studies under the TRELEGY program does not demonstrate the required quality, safety or efficacy, or that additional non-clinical or clinical studies are required with respect to the program;
- any adverse effects resulting from the COVID-19 pandemic;
- any safety, efficacy or other concerns regarding the TRELEGY program or any GSK-Partnered Respiratory Program in which we have a substantial economic interest; or
- any particular FDA requirements or changes in FDA policy or guidance regarding the TRELEGY program or any other GSK-Partnered Respiratory Program or any particular regulatory requirements in other jurisdictions or changes in the policies or guidance adopted by foreign regulatory authorities.

Because GSK is a strategic partner of Innoviva, a strategic partner of TRC and a significant shareholder of us, it may take actions that in certain cases are materially harmful to our business and to our other shareholders.

Based on our review of publicly available filings, as of December 31, 2021, GSK beneficially owned 13.0% of our outstanding ordinary shares (although GSK, through a subsidiary, has issued $280,336,000 of exchangeable senior notes due 2023 (the "GSK Notes"), initially exchangeable into 9,644,792 of our ordinary shares which, as of December 31, 2021, represented 13.0% of our outstanding ordinary shares). GSK is also a strategic partner to Innoviva with rights and obligations under the GSK Agreements, which include the strategic alliance agreement and the collaboration agreement assigned to TRC, that may cause GSK's interests to differ from our interests and those of our other shareholders. For example, GSK's commercialization efforts are guided by a portfolio approach across products in which we have an indirect interest through TRC and products in which we have no interest. Accordingly, GSK's commercialization efforts may have the effect of reducing the value of our interest in TRC. Furthermore, GSK has a substantial respiratory product portfolio in addition to the products covered by the GSK Agreements. GSK may make respiratory product portfolio decisions or statements about its portfolio which may be, or may be perceived to be, harmful to the respiratory products partnered with Innoviva and TRC. For example, GSK could promote its own respiratory products and/or delay or terminate the development or commercialization of the respiratory programs covered by the GSK Agreements, which include TRELEGY. Also, given the potential future royalty payments GSK may be obligated to pay under the GSK Agreements, GSK may seek to acquire us or acquire our interests in TRC in order to effectively reduce those payment obligations and the price at which GSK might seek to acquire us may not reflect our true value. As a result of these differing interests, GSK may take actions that it believes are in its best interest but which might not be in the best interests of either us or our other shareholders. In addition, GSK could also seek to challenge our or Innoviva's post-Spin-Off operations as violating or allowing it to terminate the GSK Agreements, including by violating the confidentiality provisions of those agreements or the master agreement between GSK, Innoviva and us entered into in connection with the Spin-Off (the "Master Agreement"), or otherwise violating its legal rights. While we

believe our operations fully comply with the GSK Agreements, the Master Agreement and applicable law, there can be no assurance that we or Innoviva will prevail against any such claims by GSK. Moreover, regardless of the merit of any claims by GSK, we may incur significant cost and diversion of resources in defending them. In addition, any other action or inaction by either GSK or Innoviva that results in a material dispute, allegation of breach, litigation, arbitration, or significant disagreement between those parties or between us and either of those parties may be interpreted negatively by the market or by our investors, could harm our business and cause the price of our securities to fall. Other examples of these kinds of issues include but are not limited to non-performance of other contractual obligations and allegations of non-performance, disagreements over the relative marketing and sales efforts for Innoviva's partnered products and other GSK respiratory products, disputes over public statements, and similar matters. In general, any uncertainty about respiratory programs partnered with GSK, the enforceability of the GSK Agreements or the relationship/partnership between Innoviva and GSK or between us and Innoviva could result in significant reduction in the market price of our securities and other material harm to our business.

We do not control the commercialization of TRELEGY and we do not control TRC; accordingly the amount of royalties we receive will depend on, among other factors, GSK's ability to further commercialize TRELEGY and TRC's decisions concerning use of cash in accordance with the TRC LLC Agreement.

We only receive revenues from TRELEGY based on the amount of sales of this product by GSK in the form of our economic interest in the royalties paid by GSK to TRC, which is managed by Innoviva. There are no required minimum future payments associated with the product and any royalties we receive will depend on GSK's ability to commercialize the product, the future payments, if any, made by GSK to TRC, TRC's expenses, and the amount of cash, if any, expected to be used by TRC pursuant to the TRC LLC Agreement. Following our 2019 arbitration with Innoviva concerning its withholding of certain royalty distributions to the TRC members, the arbitrator ruled, among other things, that in the future if Innoviva desires to invest TRC funds in any initiatives that require the consent of GSK under the collaboration agreement, Innoviva must first obtain the consent of GSK. The timeframe for seeking GSK's consent for these initiatives and the associated dates by which GSK's consent must be received means that royalty distributions could be delayed for several quarters (if GSK ultimately does not consent) or perhaps not made at all until the completion of the initiatives (to the extent that GSK does consent and agrees with TRC that TRC funding will be used for such initiatives). We initiated an arbitration proceeding in October 2020 against Innoviva and TRC, challenging the authority of Innoviva and TRC to pursue a business plan to use TRELEGY royalties to invest in certain privately-held companies, rather than distribute such funds that would otherwise be available for distribution to us under the terms of the TRC LLC Agreement to us in a manner that we believe is consistent with the TRC LLC Agreement and our 85% economic interest in TRC. On March 30, 2021, the arbitrator ruled that, we had not shown that at their then current levels of investment, Innoviva and TRC had not breached the LLC Agreement as of the date of the arbitration. The arbitrator further ruled that Innoviva and TRC had not breached the implied covenant of good faith and fair dealing; or their fiduciary duties. The arbitrator also ruled that (i) Innoviva was entitled to indemnification from TRC for all legal fees and expenses reasonably incurred in the arbitration and (ii) we were entitled to indemnification from TRC for legal fees and costs incurred in defending an action Innoviva brought against us in the Delaware Court of Chancery. The arbitrator noted in the ruling that although we failed to show that Innoviva's investment activities, at the then current levels of investment, have or will have a material and adverse effect on our economic interest in TRC, this does not mean that any future investments or actions will not require our consent. The arbitrator noted in the ruling that we may, in the future, have a consent right over the decision to continue this investment strategy or whether to make a particular investment if, for example, Innoviva develops a track record of poor investments, over allocates royalties to these investment activities, or fails to distribute sufficient investment returns, and such facts cause the strategy or investment to have a material adverse effect on our economic interest in TRC. We have objected to the proposed investments in private companies presented in draft TRC quarterly financial plans to date.

Accordingly, our economic interest in TRC LLC involves a number of risks and uncertainties, including:

- any future withholding by Innoviva or TRC of royalty distributions and decisions made by Innoviva, as TRC's manager, regarding the timing and amount of distributions;
- the amount of cash associated with any additional future investments for which Innoviva expends TRC funds;

- GSK's ability to have an adequate supply of TRELEGY product;
- ongoing compliance by GSK or its suppliers with the FDA's current Good Manufacturing Practice;
- compliance with other applicable FDA and other regulatory requirements in the US or other foreign jurisdictions, including those described elsewhere in this report;
- competition, whether from current competitors or new products developed by others in the future;
- claims relating to intellectual property;
- any future disruptions in GSK's business which would affect its ability to commercialize TRELEGY, including, disruptions due to the COVID-19 pandemic;
- the ability of TRELEGY to achieve wider acceptance among physicians, patients, third-party payors, or the medical community in general;
- the amount of cash associated with any additional future TRELEGY commercialization initiatives that Innoviva proposes to GSK for TRC to pursue, the time it may take to present those initiatives to GSK for approval and the time it takes for GSK to consent or not consent;
- global economic conditions;
- the resolution of any disputes between Innoviva and TRC, on the one hand, and us, on the other, regarding the timing of distributions, the amount of distributions, and the proper business activities of TRC; and
- any of the other risks relating to commercialization of TRELEGY.

These risks and uncertainties could materially impact the amount and timing of future royalties or other revenues we may receive from sales of TRELEGY, which could have a material adverse effect on our future revenues, other financial results and our financial position and cause the price of our securities to fall.

In the future, Innoviva may cause TRC to withhold funds from distribution to its members, including our affiliates, for purposes consistent with the 2019 and 2021 arbitration rulings, or otherwise. Accordingly, we cannot predict the amount of the funds that our affiliates would otherwise expect to receive from TRC that TRC may withhold in the future, or the timing of any such withholding.

We may object to the withholding of funds in the future on the basis that such withholding is in violation of the terms of the TRC LLC Agreement, as interpreted by the 2019 and 2021 arbitration rulings, or otherwise, and such objection could result in additional legal proceedings between us, TRC and Innoviva. Any such legal proceedings could divert the attention of management and cause us to incur significant costs, regardless of the outcome, which we cannot predict. An adverse result could materially and adversely affect the funds that our affiliates would otherwise expect to receive from TRC in the future and thus have a material adverse effect on our business, financial condition, and results of operations.

Any delay in commencing or completing clinical studies for product candidates and any adverse results from clinical or non-clinical studies or regulatory obstacles product candidates may face, would harm our business and the price of our securities could fall.

Each of our product candidates must undergo extensive non-clinical and clinical studies as a condition to regulatory approval. Non-clinical and clinical studies are expensive, take many years to complete and study results may lead to delays in further studies, new requirements for conducting future studies or decisions to terminate programs. The commencement and completion of clinical studies for our product candidates may be delayed and programs may be terminated due to many factors, including, but not limited to:

- lack of effectiveness of product candidates during clinical studies;

- adverse events, safety issues or side effects (or perceived adverse developments or results) relating to the product candidates or their formulation into medicines;
- insufficient capital to continue our development programs, some of which are which are expensive;
- inability to enter into partnering arrangements relating to the development and commercialization of our programs and product candidates or partner decisions not to maintain a partnership with us;
- delays in patient enrollment and variability in the number and types of patients available for clinical studies;
- the need to sequence clinical studies as opposed to conducting them concomitantly in order to conserve resources;
- our inability or the inability of our collaborators or licensees to manufacture or obtain from third parties materials sufficient for use in non-clinical and clinical studies;
- governmental or regulatory delays or suspensions of the conduct of the clinical trials and changes in regulatory requirements, policy and guidelines, including as a result of any class-based risks that emerge as an area of FDA or other regulatory agency focus;
- challenges related to the COVID-19 pandemic, including with recruitment and/or progressing patients through studies;
- failure of our partners to advance our product candidates through clinical development;
- difficulty in maintaining contact with patients after treatment, resulting in incomplete data;
- varying regulatory requirements or interpretations of data among the FDA and foreign regulatory authorities; and
- a disturbance where we or our collaborative partners are enrolling patients in clinical trials, such as a pandemic, terrorist activities or war, political unrest or a natural disaster.

Any adverse developments or results or perceived adverse developments or results with respect to our clinical programs including, without limitation, any delays in development in our programs, any halting of development in our programs, any difficulties or delays encountered with regard to the FDA or other third country regulatory authorities with respect to our programs, or any indication from clinical or non-clinical studies that the compounds in our programs are not safe or efficacious, could have a material adverse effect on our business and cause the price of our securities to fall. For example, in August 2021 we announced that our Phase 2b study of izencitinib in ulcerative colitis did not meet its primary endpoint and in September 2021 we announced that our four-week SEQUOIA Phase 3 study for ampreloxetine did not meet its primary endpoint.

In July 2019, the FDA issued a Boxed Warning for a systemically active pan-JAK inhibitor, calling out an increased risk of pulmonary embolism and death following the results of a safety study in patients with rheumatoid arthritis. We are planning to develop certain pan-JAK inhibitors that are designed to remain organ-selective so that they do not become systemically active in order to minimize the risk of side effects. It is unknown at this time what, if any, additional requirements the FDA may put in place with respect to the development of JAK inhibitors generally or what other future FDA actions may have on the prospects for JAK inhibitors. Delays or adverse developments or results or

perceived adverse developments or results relating to JAK inhibitors could harm our business and could cause the price of our securities to fall. Examples of such adverse developments include, but are not limited to:

- the FDA and/or other regulatory authorities determining that additional non-clinical or clinical studies are required with respect to our JAK inhibitor programs;
- safety, efficacy or other concerns relating to our JAK inhibitor programs or JAK inhibitors under development or commercialized by other companies;
- the FDA determining that class-based warnings are required for JAK inhibitors generally; or
- any change in FDA policy or guidance regarding JAK inhibitors.

If our product candidates are not approved by regulatory authorities, including the FDA, we will be unable to commercialize them.

The FDA must approve any new medicine before it can be marketed and sold in the US. We will not obtain this approval for a product candidate unless and until the FDA approves an NDA. We, or our collaborative partners, must provide the FDA and similar foreign regulatory authorities with data from preclinical and clinical studies that demonstrate that our product candidates comply with the regulatory requirements for the quality of medicinal products and are safe and effective for a defined indication before they can be approved for commercial distribution. FDA or foreign regulatory authorities may disagree with our trial design and our interpretation of data from preclinical studies and clinical trials. The processes by which regulatory approvals are obtained from the FDA and foreign regulatory authorities to market and sell a new product are complex, require a number of years, depend upon the type, complexity and novelty of the product candidate and involve the expenditure of substantial resources for research, development and testing. The FDA has substantial discretion in the drug approval process and may require us to conduct additional non-clinical and clinical testing or to perform post-marketing studies. Further, the implementation of new laws and regulations, and revisions to FDA clinical trial design guidance may lead to increased uncertainty regarding the approvability of new drugs. See the risk factor entitled "*Any delay in commencing or completing clinical studies for product candidates and any adverse results from clinical or non-clinical studies or regulatory obstacles product candidates may face, would harm our business and the price of our securities could fall*" above for additional information. The rapidly shifting environment surrounding the collective response to the COVID-19 pandemic has led to additional guidance from US and foreign regulatory agencies with respect to numerous matters regarding the conduct of clinical trials in general and the development of COVID-19 related therapies, which is subject to the risk of further change, misinterpretation or non-compliance due to the rapidly changing regulatory landscape. In addition, the FDA has additional standards for approval of new drugs, including recommended advisory committee meetings for certain new molecular entities, and formal risk evaluation and mitigation requirements at the FDA's discretion. Even if we receive regulatory approval of a product, the approval may limit the indicated uses for which the drug may be marketed or impose significant restrictions or limitations on the use and/or distribution of such product.

In addition, in order to market our medicines in foreign jurisdictions, we or our collaborative partners must obtain separate regulatory approvals in each country. The approval procedure varies among countries and can involve additional testing, and the time required to obtain approval may differ from that required to obtain FDA approval. Approval by the FDA does not ensure approval by regulatory authorities in other countries, and approval by one foreign regulatory authority does not ensure approval by regulatory authorities in other foreign countries or by the FDA. Conversely, failure to obtain approval in one or more jurisdictions may make approval in other jurisdictions more difficult. These laws, regulations, additional requirements and changes in interpretation could cause non-approval or further delays in the FDA's or other regulatory authorities' review and approval of our and our collaborative partner's product candidates, which would materially harm our business and financial condition and could cause the price of our securities to fall.

If sufficient capital is not available, we may have to further curtail operations or we could be forced to share our rights to commercialize our product candidates with third parties on terms that may not be favorable to us.

Based on our current operating plans and financial forecasts, we believe that our existing cash, cash equivalents and marketable securities will be sufficient to meet our anticipated operating needs for at least the next twelve months. However, our current operating plans or financial forecasts occasionally change. For example, in August 2017, we announced an increase in our anticipated operating loss for 2017, primarily driven by our decision to accelerate funding associated with the next phase of development of izencitinib in our JAK inhibitor program. In addition, following unfavorable results from our late-stage development programs, in September 2021, we announced a strategic update and corporate restructuring (the "Restructuring") to focus on leveraging our expertise in developing and commercializing respiratory therapeutics, including a reduction in headcount by approximately 75% through a reduction in our workforce of regular and contingent workers. If our current operating plans or financial forecasts change, we may require or seek additional funding sooner in the form of public or private equity or equity-linked offerings, debt financings or additional collaborations and licensing arrangements.

We may need to raise additional capital in the future to, among other things:

- fund our discovery efforts and research and development programs;
- fund our commercialization strategies for any approved products and to prepare for potential product approvals;
- support our independent sales and marketing organization and medical affairs team;
- support our additional investments in YUPELRI, including post-marketing clinical studies;
- progress any additional product candidates into later-stage development without funding from a collaboration partner;
- progress mid-to-late stage product candidates into later-stage development, if warranted;
- respond to competitive pressures; and
- acquire complementary businesses or technologies.

Our future capital needs depend on many factors, including:

- the scope, duration and expenditures associated with our discovery efforts and research and development programs;
- continued scientific progress in these programs;
- the extent to which we encounter technical obstacles in our research and development programs;
- the outcome of potential licensing or partnering transactions, if any;
- competing technological developments;
- the extent of our proprietary patent position in any approved products and our product candidates;
- our facilities expenses, which will vary depending on the time and terms of any facility lease or sublease we may enter into, and other operating expenses;
- the scope and extent of the expansion of our sales and marketing efforts;

- potential litigation and other contingencies; and
- the regulatory approval process for our product candidates.

We may seek to raise additional capital or obtain future funding through public or private equity offerings, debt financings or additional collaborations and licensing arrangements to meet our capital needs or to take advantage of opportunistic market conditions. We may not be able to obtain additional financing on terms favorable to us, if at all. General market conditions may make it difficult for us to seek financing from the capital markets. We may be required to relinquish rights to our technologies, product candidates or territories, or grant licenses on terms that are not favorable to us, in order to raise additional funds through collaborations or licensing arrangements. We may sequence preclinical and clinical studies as opposed to conducting them concomitantly in order to conserve resources, or delay, reduce or eliminate one or more of our research or development programs and reduce overall overhead expenses. If we are unable to raise additional capital or obtain future funding in sufficient amounts or on terms acceptable to us, we may have to make reductions in our workforce and may be prevented from continuing our discovery, development and commercialization efforts and exploiting other corporate opportunities. This would likely harm our business, prospects and financial condition and cause the price of our securities to fall.

We may seek to obtain future financing through the issuance of debt or equity, which may have an adverse effect on our shareholders or may otherwise adversely affect our business.

We may in the future need to raise additional funds to continue to progress our business. If we raise funds through the issuance of additional debt, including convertible debt or debt secured by some or all of our assets, or equity, any debt securities or preferred shares issued will have rights, preferences and privileges senior to those of holders of our ordinary shares in the event of liquidation. Neither the terms of our $230.0 million of 3.25% convertible senior notes, due 2023 (the "Convertible Senior 2023 Notes") nor the terms of the Issuer II's 9.5% Fixed Rate Term Notes due on or before 2035 (the "Non-Recourse 2035 Notes") restrict our ability to issue additional debt. If additional debt is issued or we otherwise borrow additional funds, there is a possibility that once all senior claims are settled, there may be no assets remaining to pay out to the holders of ordinary shares. Moreover, 75% of the income from our investment in TRC, as evidenced by the Issuer II Class C Units, is currently available only for payment of the Non-Recourse 2035 Notes and is not available to pay our other obligations or the claims of our other creditors. Additionally, the conversion price of our Convertible Senior 2023 Notes is $34.45 per share and as of December 31, 2021, we had cash, cash equivalents and short-term marketable securities of $173.5 million. If the trading price of our ordinary shares does not exceed this amount, we would be required to repay or refinance the Convertible Senior 2023 Notes, and we cannot assure you that we would be able to do so. In addition, if we raise funds through the issuance of additional equity, whether through private placements or public offerings, such an issuance would dilute ownership of our current shareholders that do not participate in the issuance. If we are unable to obtain any needed additional funding, we may be required to reduce the scope of, delay, or eliminate some or all of, our planned research, development and commercialization activities or to license to third parties the rights to develop and/or commercialize products or technologies that we would otherwise seek to develop and/or commercialize ourselves or on terms that are less attractive than they might otherwise be, any of which could materially harm our business.

Furthermore, the terms of any additional debt securities we may issue in the future may impose restrictions on our operations, which may include limiting our ability to incur additional indebtedness, pay dividends on or repurchase our share capital, or make certain acquisitions or investments. In addition, we may be subject to covenants requiring us to satisfy certain financial tests and ratios, and our ability to satisfy such covenants may be affected by events outside of our control.

If our partners do not satisfy their obligations under our agreements with them, or if they terminate our partnerships with them, we may not be able to develop or commercialize our partnered product candidates as planned.

In January 2015, we entered into a collaboration agreement with Viatris for the development and commercialization of a nebulized formulation of our LAMA revefenacin, including YUPELRI. Under the terms of the agreement, we and Viatris will co-develop nebulized revefenacin, including YUPELRI, for COPD and other respiratory diseases. In June 2016, we entered into a License and Collaboration Agreement with Millennium Pharmaceuticals, Inc.,

an indirect wholly-owned subsidiary of Takeda Pharmaceutical Company Limited (collectively with Millennium, "Takeda") in order to establish a collaboration for the development and commercialization of TD-8954, a selective 5-HT4 receptor agonist in development for gastrointestinal motility disorders. In December 2019, we entered into a License Agreement with Pfizer Inc. ("Pfizer"). Under the license agreement, we provide Pfizer with an exclusive global license to develop, manufacture and commercialize compounds from our preclinical program for skin-targeted, locally-acting pan-Janus kinase (JAK) inhibitors that can be rapidly metabolized. We also have an exclusive development and commercialization agreement with Alfasigma for velusetrag, our internally discovered 5-HT4 agonist for the treatment of gastromotility disorders, under which we have transferred to Alfasigma global rights for velusetrag. In connection with these agreements, these parties have certain rights regarding the use of patents and technology with respect to the compounds in our development programs, including development and marketing rights.

Our partners have in the past and may in the future not fulfill all of their obligations under these agreements, and, in certain circumstances, they or we may terminate our partnership with them. In addition, our partners may also be facing significant business interruptions as a result of the COVID-19 pandemic. In either event, we may be unable to assume the development and commercialization responsibilities covered by the agreements or enter into alternative arrangements with a third-party to develop and commercialize such product candidates. If a partner elected to promote alternative products and product candidates such as its own products and product candidates in preference to those licensed from us, does not devote an adequate amount of time and resources to our product candidates or is otherwise unsuccessful in its efforts with respect to our products or product candidates, the development and commercialization of product candidates covered by the agreements could be delayed or terminated, and future payments to us could be delayed, reduced or eliminated and our business and financial condition could be materially and adversely affected. Accordingly, our ability to receive any revenue from the product candidates covered by these agreements is dependent on the efforts of our partners. If a partner terminates or breaches its agreements with us, otherwise fails to complete its obligations in a timely manner or alleges that we have breached our contractual obligations under these agreements, the chances of successfully developing or commercializing product candidates under the collaboration could be materially and adversely affected. In addition, effective collaboration with a partner requires coordination to achieve complex and detail-intensive goals between entities that potentially have different priorities, capabilities and processes and successful navigation of the challenges such coordination entails. We could also become involved in disputes with a partner, which could lead to delays in or termination of our development and commercialization programs and time-consuming and expensive litigation or arbitration. Furthermore, termination of an agreement by a partner could have an adverse effect on the price of our ordinary shares or other securities even if not material to our business.

Our ongoing drug discovery and development efforts might not generate additional successful product candidates or approvable drugs.

Our compounds in clinical trials and our future leads for potential drug compounds are subject to the risks and failures inherent in the development of pharmaceutical products. These risks include, but are not limited to, the inherent difficulty in selecting the right drug and drug target and avoiding unwanted side effects, as well as unanticipated problems relating to product development, testing, enrollment, obtaining regulatory approvals, maintaining regulatory compliance, manufacturing, competition and costs and expenses that may exceed current estimates.

Clinical studies involving our product candidates may reveal that those candidates are ineffective, inferior to existing approved medicines, unacceptably toxic, or that they have other unacceptable side effects. In addition, the results of preclinical studies do not necessarily predict clinical success, and larger and later-stage clinical studies may not produce the same results as earlier-stage clinical studies. For example, despite promising early stage studies, we recently announced that two late stage clinical programs failed to meet their primary endpoints and we now no longer plan to continue to pursue the development programs for those compounds as planned.

Frequently, product candidates that have shown promising results in early preclinical or clinical studies have subsequently suffered significant setbacks or failed in later non-clinical or clinical studies. In some instances, there can be significant variability in safety and/or efficacy results between different trials of the same product candidate due to numerous factors, including changes in trial protocols, differences in size and type of the patient populations, varying levels of adherence to the dosing regimen and other trial protocols and the rate of dropout among clinical trial participants. Clinical and non-clinical studies of product candidates often reveal that it is not possible or practical to continue development efforts for these product candidates. In addition, the design of a clinical trial can determine

whether its results will support regulatory approval and flaws in the design of a clinical trial may not become apparent until the clinical trial is well underway or completed. As our clinical studies for two of our current product candidates suggested that our product candidates were not efficacious in the indications we were investigating, we choose to cease development of these product candidates and are currently winding down our development programs for these product candidates. In addition, our product candidates may have undesirable side effects or other unexpected characteristics that could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in a more restricted label or the delay or denial of regulatory approval by regulatory authorities.

We face substantial competition from companies with more resources and experience than we have, which may result in others discovering, developing, receiving approval for or commercializing products before or more successfully than we do.

Our ability to succeed in the future depends on our ability to demonstrate and maintain a competitive advantage with respect to our approach to the discovery, development and commercialization of medicines. Our objective is to discover, develop and commercialize new small molecule medicines with superior efficacy, convenience, tolerability and/or safety using our proprietary insight in chemistry, biology and multivalency, where applicable. We expect that any medicines that we commercialize with or without our collaborative partners will compete with existing or future market-leading medicines.

Many of our current and potential competitors have substantially greater financial, technical and personnel resources than we have. In addition, many of these competitors have significantly greater commercial infrastructures than we have. Our ability to compete successfully will depend largely on our ability to leverage our experience in drug discovery and development, and, more recently, commercialization, to:

- discover and develop medicines that are superior to other products in the market;
- attract and retain qualified personnel;
- obtain and enforce patent and/or other proprietary protection for our medicines and technologies;
- conduct effective clinical trials and obtain required regulatory approvals;
- develop and effectively implement commercialization strategies, with or without collaborative partners; and
- successfully collaborate with pharmaceutical companies in the discovery, development and commercialization of new medicines.

Pharmaceutical companies, including companies with which we collaborate, may invest heavily to quickly discover and develop or in-license novel compounds that could make our product candidates obsolete. Accordingly, our competitors may succeed in obtaining patent protection, receiving FDA or equivalent regulatory approval outside the US or discovering, developing and commercializing medicines before we do. Other companies are engaged in the discovery of medicines that would compete with the product candidates that we are developing.

Any new medicine that competes with a generic or proprietary market leading medicine must demonstrate compelling advantages in efficacy, convenience, tolerability and/or safety in order to overcome severe price competition and be commercially successful. For example, YUPELRI competes predominantly with the nebulized LAMA Lonhala® Magnair® (glycopyrrolate) dosed two times per day and with short acting nebulized bronchodilators that are dosed three to four times per day. If we are not able to compete effectively against our current and future competitors, our business will not grow, our financial condition and operations will suffer and the price of our securities could fall.

If we are unable to enter into future collaboration arrangements or if any such collaborations with third parties are unsuccessful, we will be unable to fully develop and commercialize all of our product candidates and our business will be adversely affected.

We have collaborations with a number of third parties including Viatris for the development and commercialization of a nebulized formulation of revefenacin, our LAMA compound (including YUPELRI). Also, through our interest in TRC we may participate economically in Innoviva's collaborations with GSK with respect to the GSK-Partnered Respiratory Programs. Additional collaborations will likely be needed to fund later-stage development of certain programs that have not been licensed to a collaborator and to commercialize the product candidates in our programs if approved by the necessary regulatory authorities. We evaluate commercial strategy on a product by product basis either to engage pharmaceutical or other healthcare companies with an existing sales and marketing organization and distribution system to market, sell and distribute our products or to commercialize a product ourselves. However, we may not be able to establish these sales and distribution relationships on acceptable terms, or at all, or may encounter difficulties in commercializing a product ourselves. For any of our product candidates that receive regulatory approval in the future and are not covered by our current collaboration agreements, we will need a partner in order to commercialize such products unless we establish independent sales, marketing and distribution capabilities with appropriate technical expertise and supporting infrastructure.

Collaborations with third parties regarding our programs may require us to relinquish material rights, including revenue from commercialization of our medicines, or to assume material ongoing development obligations that we would have to fund. These collaboration arrangements are complex and time-consuming to negotiate, and if we are unable to reach agreements with third-party collaborators, we may fail to meet our business objectives and our financial condition may be adversely affected. We face significant competition in seeking third-party collaborators. We may be unable to find third parties to pursue product collaborations on a timely basis or on acceptable terms. Furthermore, for any collaboration, we may not be able to control the amount of time and resources that our partners devote to our product candidates and our partners may choose to prioritize alternative programs or otherwise be unsuccessful in their efforts with respect to our products or product candidates. In addition, effective collaboration with a partner requires coordination to achieve complex and detail-intensive goals between entities that potentially have different priorities, capabilities and processes and successful navigation of the challenges such coordination entails. For example, Viatris has a substantial existing product portfolio and other considerations that influence its resource allocation, and other priorities and internal organizational processes that differ from our own. As a result of these differing interests and processes, Viatris may take actions that it believes are in its best interest but which might not be in the best interests of either us or our other shareholders. Our inability to successfully collaborate with third parties would increase our development costs and may cause us to choose not to continue development of certain product candidates, would limit the likelihood of successful commercialization of some of our product candidates, may cause us not to continue commercialization of our authorized products and could cause the price of our securities to fall.

We depend on third parties in the conduct of our non-clinical and clinical studies for our product candidates.

We depend on independent clinical investigators, contract research and manufacturing organizations and other third-party service providers in the conduct of our non-clinical and clinical studies for our product candidates. We rely heavily on these parties for execution of our non-clinical and clinical studies, and control only certain aspects of their activities. Nevertheless, we are responsible for ensuring that our clinical studies are conducted in accordance with good clinical, laboratory and manufacturing practices ("GXPs") and other regulations as required by the FDA and foreign regulatory authorities, and the applicable protocol. Failure by these parties to comply with applicable regulations and practices in conducting studies of our product candidates can result in a delay in our development programs or non-approval of our product candidates by regulatory authorities. Furthermore, to the extent the operations of these third parties are disrupted as result of the COVID-19 pandemic or otherwise, our development programs could be delayed.

The FDA, and equivalent authorities in third countries, enforces GXPs and other regulations through periodic inspections of trial sponsors, clinical research organizations ("CROs"), principal investigators and trial sites. If we or any of the third parties on which we have relied to conduct our clinical studies are determined to have failed to comply with GXPs (or other equivalent regulations outside the US), the study protocol or applicable regulations, the clinical data generated in our studies may be deemed unreliable. This could result in non-approval of our product candidates by the FDA, or equivalent authorities in other countries, or we, the FDA, or equivalent authorities in other countries may decide

to conduct additional audits or require additional clinical studies, which would delay our development programs, could result in significant additional costs and cause the price of our securities to fall.

There is a single source of supply for a number of our product candidates and for YUPELRI, and our business will be harmed if any of these single-source manufacturers are not able to satisfy demand and alternative sources are not available.

We have limited in-house production capabilities for preclinical and clinical study purposes and depend primarily on a number of third-party Active Pharmaceutical Ingredient ("API") and drug product manufacturers. We may not have long-term agreements with these third parties and our agreements with these parties may be terminable at will by either party at any time. In addition, there is a single supplier of YUPELRI API and a single supplier of YUPELRI drug product. If, for any reason, any of these third-party manufacturers are unable or unwilling to perform, or if their performance does not meet regulatory requirements, alternative manufacturers may not be available or may not be available on acceptable terms. Any inability to acquire sufficient quantities of API and drug product in a timely manner from these third parties could delay preclinical and clinical studies, prevent us from developing our product candidates in a cost-effective manner or on a timely basis or adversely impact the commercialization of YUPELRI. In addition, manufacturers of our API and drug product are subject to the FDA's current Good Manufacturing Practice ("cGMP") regulations and similar foreign standards and we do not have control over compliance with these regulations by our manufacturers.

Our manufacturing strategy presents the following additional risks:

- because of the complex nature of many of our compounds, our manufacturers may not be able to successfully manufacture our APIs and/or drug products in a cost-effective and/or timely manner and changing manufacturers for our APIs or drug products could involve lengthy technology transfer, validation and regulatory qualification activities for the new manufacturer;

- the processes required to manufacture certain of our APIs and drug products are specialized and available only from a limited number of third-party manufacturers;

- some of the manufacturing processes for our APIs and drug products have not been scaled to quantities needed for continued clinical studies or commercial sales, and delays in scale-up to higher quantities could delay clinical studies, regulatory submissions and commercialization of our product candidates; and

- because some of the third-party manufacturers are located outside of the US, there may be difficulties in importing our APIs and drug products or their components into the US as a result of, among other things, FDA import inspections, incomplete or inaccurate import documentation or defective packaging.

We have a significant amount of debt, including our Non-Recourse 2035 Notes and Convertible Senior 2023 Notes, that are senior in capital structure and cash flow, respectively, to holders of our ordinary shares. Satisfying the obligations relating to our debt could adversely affect the amount or timing of distributions to our shareholders.

As of December 31, 2021, we had $654.8 million in total long-term liabilities outstanding, comprised primarily of $375.7 million in net principal that remains outstanding under the Issuer II's (defined below) Non-Recourse 2035 Notes and $230.0 million in principal that remains outstanding under our Convertible Senior 2023 Notes (together with the Non-Recourse 2035 Notes, the "Notes").

The Convertible Senior 2023 Notes are unsecured debt and are not redeemable by us prior to the maturity date except for certain changes in tax law. Holders of the Convertible Senior 2023 Notes may require us to purchase all or any portion of their notes at 100% of their principal amount, plus any unpaid interest, upon a fundamental change such as a change of control of us or the termination of trading of our ordinary shares in accordance with the indenture governing the Convertible Senior 2023 Notes.

Until the Non-Recourse 2035 Notes are paid in full, holders of the Non-Recourse 2035 Notes have a perfected security interest in the Issuer II Class C Units that represent a 63.75% economic interest in any future payments that may be made by GSK to TRC under the strategic alliance agreement and under the portion of the collaboration agreement

assigned to TRC by Innoviva (net of TRC expenses paid and the amount of cash, if any, expected to be used by TRC pursuant to the TRC LLC Agreement over the next four fiscal quarters) relating to the GSK-Partnered Respiratory Programs, including the TRELEGY program.

Prior to and including the December 5, 2024 payment date, the terms of the Non-Recourse 2035 Notes provide that in the event that the distributions received by the Issuer II from TRC in a quarter is less than the interest accrued for that quarter, the principal amount of the Non-Recourse 2035 Notes will increase by the interest shortfall amount for that quarter. The terms of the Non-Recourse 2035 Notes also provide that Theravance Biopharma, at its option, may satisfy the quarterly interest payment obligations by making a capital contribution to the Issuer II.

Satisfying the obligations of these Notes could adversely affect the amount or timing of any distributions to our shareholders. In addition, the Non-Recourse 2035 Notes may be redeemed by Issuer II on and after February 28, 2022, in whole or in part, at specified redemption premiums. We may further choose to satisfy, repurchase, or refinance any Non-Recourse 2035 Notes, to the extent allowable, through public or private equity or debt financings if we deem such financings are available on favorable terms. If any or all of the Convertible Senior 2023 Notes are not converted into our ordinary shares before the maturity date, we will have to pay the holders the full aggregate principal amount of the Convertible Senior 2023 Notes then outstanding. If the Non-Recourse 2035 Notes are not refinanced or paid in full the holders of the Non-Recourse 2035 Notes will have the right to foreclose on the Issuer II Class C Units that represent a 63.75% economic interest in future royalties due on net sales of TRELEGY and related assets. If the Issuer II Class C Units are foreclosed upon, we will lose any right to receive 75% of the future royalty payments made by GSK in connection with the net sales of TRELEGY and related assets. Any of the above payments could have a material adverse effect on our cash position. Our failure to satisfy these obligations may result in a default under the applicable indenture governing these Notes, which could result in a default under certain of our other debt instruments, if any. Any such default would harm our business and the price of our securities could fall. For more information, see Part II—Item 7—Management's Discussion and Analysis of Financial Condition and Results of Operations—Liquidity and Capital Resources**.**

Servicing our Convertible Senior 2023 Notes requires a significant amount of cash, and we may not have sufficient cash flow from our business to pay our debt. Additionally, holders may require us to repurchase our Convertible Senior 2023 Notes under certain circumstances, and we may not have sufficient cash to do so.

Our ability to make interest or principal payments when due or to refinance the Convertible Senior 2023 Notes depends on our future performance, which is subject to economic, financial, competitive and other factors beyond our control. Our business may not generate cash flow from operations sufficient to satisfy our obligations under the Convertible Senior 2023 Notes and any future indebtedness we may incur and to make necessary capital expenditures. In addition, the issuance of the Non-Recourse 2035 Notes reduced the cash available for us to make interest or principal payments on, or to refinance, the Convertible Senior 2023 Notes. We may be required to adopt one or more alternatives, such as reducing or delaying investments or capital expenditures, selling assets, refinancing or obtaining additional equity capital on terms that may be onerous or highly dilutive. Our ability to refinance the Convertible Senior 2023 Notes or future indebtedness will depend on the capital markets and our financial condition at such time. We may not be able to engage in any of these activities on desirable terms or at all, which could result in a default on the Convertible Senior 2023 Notes or future indebtedness.

The holders of the Convertible Senior 2023 Notes may have the right to require us to repurchase the Convertible Senior 2023 Notes upon the occurrence of a "fundamental change" such as a change of control of our Company or the termination of trading of our ordinary shares, as defined in the indenture governing the Convertible Senior 2023 Notes. We may not have sufficient funds to repurchase the Convertible Senior 2023 Notes in cash or have the ability to arrange necessary financing on acceptable terms. Our failure to repurchase the Convertible Senior 2023 Notes when required would result in an event of default with respect to the Convertible Senior 2023 Notes. In addition, any acceleration of the repayment of the Convertible Senior 2023 Notes or future indebtedness after any applicable notice or grace periods could have a material adverse effect on our business, results of operations and financial condition.

We may fail to achieve the expected cost savings and related benefits from our September 2021 Restructuring.

In September 2021, our Board approved a plan to restructure the Company's business operations to drive long term sustainable revenue growth, better align resources, improve operational efficiencies and to increase profitability. Upon the completion of this Restructuring, our management and employees will be primarily focused on managing our most promising respiratory programs and the size of the Company will be reduced. As part of the Restructuring, we are eliminating approximately 270 positions, or 75% of our workforce. We expect to incur total estimated Restructuring expenses and related expenses of approximately $32.0 comprised of $17.0 million in cash expenses and $15.0 million in non-cash expenses. The Restructuring and related expenses are primarily comprised of severance, retention, and other costs relating to the Restructuring and are expected to be incurred through the third quarter of 2022. Affected employees have received notification and are eligible to receive severance payments based on their responsibilities within the organization and years of service, contingent upon effectiveness of an affected employee's a separation agreement, which includes a general release of claims against us.

Overall, we expect to realize estimated operating expense savings of approximately $170.0 million (excluding share-based compensation and any one-time restructuring, severance, and termination costs). These estimates are subject to a number of assumptions, and actual results may differ. We may also incur additional costs not currently contemplated due to events that may occur as a result of, or that are associated with, the Restructuring.

We may fail to effectively execute on our Restructuring or our plans may change as we continue to optimize our asset portfolio to maximize shareholder value. These actions may take more time than we currently estimate and we may not be able to drive long term sustainable revenue growth, better align resources, improve operational efficiencies and to increase profitability. Any failure to properly execute our Restructuring could cause us not to achieve the expected benefits of these actions, and adversely affect our financial condition.

If we lose key management or scientific personnel, or if we fail to attract and retain key employees, our ability to discover and develop our product candidates and commercialize our products, if any, will be impaired.

We are highly dependent on principal members of our management team and scientific staff, and in particular, our Chief Executive Officer, Rick E Winningham, to operate our business. Mr. Winningham has significant pharmaceutical industry experience. The loss of Mr. Winningham's services could impair our ability to discover, develop and commercialize new medicines.

If we fail to retain our qualified personnel or replace them when they leave, we may be unable to continue our discovery, development and commercialization activities, which may cause the price of our securities to fall. The Restructuring announced in September 2021 may make retention of our current personnel both more important and more challenging.

In addition, our US operating subsidiary's facility and most of its employees are located in northern California, headquarters to many other biotechnology and biopharmaceutical companies and many academic and research institutions. As a result, competition for certain skilled personnel in our market is intense. None of our employees have employment commitments for any fixed period of time and they all may leave our employment at will. If we fail to retain our qualified personnel or replace them when they leave, we may be unable to continue our development and commercialization activities and the price of our securities could fall.

Our business and operations would suffer in the event of significant disruptions of information technology systems or security breaches.

We rely extensively on computer systems to maintain information and manage our finances and business. In the ordinary course of business, we collect, store and transmit large amounts of confidential information (including but not limited to trade secrets or other intellectual property, proprietary business information and personal information) and it is critical that we maintain the confidentiality and integrity of such confidential information. Although we have security measures in place, our internal information technology systems and those of our CROs and other service providers, including cloud based and hosted applications, data and services, may be vulnerable to service interruptions and security breaches from inadvertent or intentional actions by our employees, service providers and/or business partners, from cyber attacks by malicious third parties, including but not limited to those involving malware and ransomware, which can disrupt operations significantly, and/or from, natural disasters, terrorism, war and telecommunication and electrical

failures. Cyber attacks are increasing in their frequency, sophistication, and intensity, and have become increasingly difficult to detect. Significant disruptions of information technology systems or security breaches could adversely affect our business operations and result in financial, legal, business and reputational harm to us, including significant liability and/or significant disruption to our business. If a disruption of information technology systems or security breach results in a loss of or damage to our data or regulatory applications, unauthorized access, use, or disclosure of, or the prevention of access to, confidential information, or other harm to our business, we could incur liability and reputational harm, we could be required to comply with federal and/or state breach notification laws and foreign law equivalents, we may incur legal expenses to protect our confidential information, the further development of our product candidates could be delayed and the price of our securities could fall. For example, the loss of clinical trial data from completed or ongoing clinical trials of our product candidates could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. As another example, we may incur penalties imposed by the competent authorities in the EU Member States in case of breach of the EU rules governing the collection and processing of personal data, including unauthorized access to or disclosure of personal data. Although we have security and fraud prevention measures in place, we have been subject to immaterial payment fraud activity. In 2017, we filed a lawsuit (which has since been resolved) against a former employee for misappropriation of our confidential, proprietary and trade secret information. Moreover, there can be no assurance that our security measures will prevent service interruptions or security breaches that could adversely affect our business. These same risks also apply to our partners and vendors, who similarly hold sensitive and critical information related to our business in computer systems and are similarly potentially vulnerable to service interruptions and security breaches.

Global economic, political and social conditions may harm our ability to do business, increase our costs and negatively affect our stock price.

Worldwide economic conditions remain uncertain due to the United Kingdom's ("UK") recent withdrawal from the EU (often referred to as "Brexit"), current global economic challenges, the COVID-19 pandemic, and other disruptions to global and regional economies and markets.

Brexit has created significant uncertainty about the future relationship between the UK and the EU, including with respect to the laws and regulations that will apply as the UK determines which EU laws to replace or replicate after withdrawal. From a regulatory perspective, the UK's withdrawal bears significant complexity and risks.

In light of the fact that a significant portion of the regulatory framework in the UK is derived from EU laws, Brexit could materially impact the regulatory regime governing development, manufacture, importation, approval and commercialization of our product candidates in the UK or the EU. For example, a marketing authorization for a medicinal product granted by the European Commission or by the competent authorities of EU member states will no longer encompass the UK. A separate authorization granted by the UK competent authorities will be required to place medicinal products on the UK market. In addition, the UK's withdrawal from the EU affects manufacturing sites that hold an EU manufacturing authorization issued by the UK competent authorities which could impact our ability to rely on UK manufacturing sites to supply medicinal products intended for the EU market will depend on. All of these changes could increase our costs and otherwise adversely affect our business. In addition, currency exchange rates for the British Pound and the Euro with respect to each other and to the US dollar have already been, and may continue to be, negatively affected by Brexit, which could cause volatility in our quarterly financial results.

Further, development of our product candidates and/or regulatory approval may be delayed for other political events beyond our control. For example, a US federal government shutdown or budget sequestration, such as ones that occurred during 2013, 2018, and 2019, may result in significant reductions to the FDA's budget, employees and operations, which may lead to slower response times and longer review periods, potentially affecting our ability to progress development of our product candidates or obtain regulatory approval for our product candidates. Further, future government shutdowns could impact our ability to access the public markets and obtain necessary capital in order to properly capitalize and continue our operations.

Our operations also depend upon favorable trade relations between the US and those foreign countries in which our materials suppliers have operations. A protectionist trade environment in either the US or those foreign countries in which we do business, such as a change in the current tariff structures, export compliance or other trade policies, may materially and adversely affect our operations.

External factors, such as potential terrorist attacks, acts of war, geopolitical and social turmoil or similar events in many parts of the world, could also prevent or hinder our ability to do business, increase our costs and negatively affect our stock price. These geopolitical, social and economic conditions could harm our business.

Our US operating subsidiary's facility is located near known earthquake fault zones, and the occurrence of an earthquake, extremist attack or other catastrophic disaster could cause damage to our facilities and equipment, which could require us to cease or curtail operations.

Our US operating subsidiary's facility is located in the San Francisco Bay Area near known earthquake fault zones and therefore will be vulnerable to damage from earthquakes. In October 1989, a major earthquake struck this area and caused significant property damage and a number of fatalities. We are also vulnerable to damage from other types of disasters, including power loss, attacks from extremist organizations, fire, floods, communications failures and similar events. If any disaster were to occur, our ability to operate our business could be seriously impaired. In addition, the unique nature of our research activities and of much of our equipment could make it difficult and costly for us to recover from this type of disaster. We may not have adequate insurance to cover our losses resulting from disasters or other similar significant business interruptions and we do not plan to purchase additional insurance to cover such losses due to the cost of obtaining such coverage. Any significant losses that are not recoverable under our insurance policies could seriously impair our business and financial condition, which could cause the price of our securities to fall.

If YUPELRI does not continue to be accepted by physicians, patients, third-party payors, or the medical community in general, we may not receive significant additional revenues from sales of this product.

The commercial success of YUPELRI depends upon its acceptance by physicians, patients, third-party payors and the medical community in general. YUPELRI may not continue to be accepted by these parties. YUPELRI competes predominantly with the nebulized LAMA Lonhala® Magnair® (glycopyrrolate) dosed two times per day and with short acting nebulized bronchodilators that are dosed three to four times per day. We have seen increased volatility in sales of YUPELRI coinciding with the suspension of in-person sales calls, having less access to physicians and other healthcare providers and the progression of the COVID-19 pandemic and, if physicians, patients, third-party payors, or the medical community in general believe that nebulized therapy presents a risk of further spreading COVID-19 or that YUPELRI is otherwise not a preferred treatment option for those with COPD, we may see long-term declines. Shifts to novel marketing tactics are being deployed in an effort to keep awareness levels and business generation positive, but these untested and unvalidated tactics may not be effective at maintaining YUPELRI brand growth. If YUPELRI's acceptance does not continue to grow, or declines from previous levels, our business and financial results could be materially harmed.

In collaboration with Viatris, we are responsible for marketing and sales of YUPELRI in the US, which subjects us to certain risks.

We currently maintain a sales force in the US and plan to continue to augment our sales and marketing personnel to support our co-promotion obligations for YUPELRI under our agreement with Viatris. The risks of fulfilling our US co-promotion obligations to Viatris include:

- costs and expenses associated with maintaining an independent sales and marketing organization with appropriate technical expertise and supporting infrastructure, including third-party vendor logistics and consultant support, which costs and expenses could, depending on the scope and method of the marketing effort, exceed any product revenue for several years;
- our ability to retain effective sales and marketing personnel and medical science liaisons in the US;
- the ability of our sales and marketing personnel to obtain access to and educate adequate numbers of prescribers about prescribing YUPELRI, in appropriate clinical situations; and
- the lack of complementary products to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines.

If we are not successful in maintaining a sales and marketing organization with appropriate experience, technical expertise, supporting infrastructure and the ability to obtain access to and educate adequate numbers of physicians about prescribing YUPELRI in appropriate clinical situations, we will have difficulty maintaining effective commercialization of YUPELRI in the hospital setting, which would adversely affect our business and financial results and the condition and the price of our securities could fall.

We are subject to extensive and ongoing regulation, oversight and other requirements by the FDA and failure to comply with these regulations and requirements may subject us to penalties that may adversely affect our financial condition or our ability to commercialize any approved products.

Prescription drug advertising and promotion are closely scrutinized by the FDA, including substantiation of promotional claims, disclosure of risks and safety information, and the use of themes and imagery in advertising and promotional materials. As with all companies selling and marketing products regulated by the FDA in the US, we are prohibited from promoting any uses of an approved product, such as YUPELRI, that are outside the scope of those uses that have been expressly approved by the FDA as safe and effective on the product's label.

The manufacturing, labeling, packaging, adverse event reporting, advertising, promotion and recordkeeping for an approved product remain subject to extensive and ongoing regulatory requirements. If we become aware of previously unknown problems with an approved product in the US or overseas or at a contract manufacturer's facilities, a regulatory authority may impose restrictions on the product, the contract manufacturers or on us, including requiring us to reformulate the product, conduct additional clinical studies, change the labeling of the product, withdraw the product from the market or require the contract manufacturer to implement changes to its facilities.

We are also subject to regulation by regional, national, state and local agencies, including the Department of Justice, the Federal Trade Commission, the Office of Inspector General of the US Department of Health and Human Services ("OIG") and other regulatory bodies with respect to any approved product, such as YUPELRI, as well as governmental authorities in those foreign countries in which any product is approved for commercialization. The Federal Food, Drug, and Cosmetic Act, the Public Health Service Act and other federal and state statutes and regulations govern to varying degrees the research, development, manufacturing and commercial activities relating to prescription pharmaceutical products, including non-clinical and clinical testing, approval, production, labeling, sale, distribution, import, export, post-market surveillance, advertising, dissemination of information and promotion. If we or any third parties that provide these services for us are unable to comply, we may be subject to regulatory or civil actions or penalties that could significantly and adversely affect our business.

Regulatory approval for our product candidates, if any, may include similar or other limitations on the indicated uses for which we can market our medicines or the patient population that may utilize our medicines, which may limit the market for our medicines or put us at a competitive disadvantage relative to alternative therapies.

Failure to satisfy required post-approval requirements and/or commitments may have implications for a product's approval and may carry civil monetary penalties. Any failure to maintain regulatory approval will materially limit the ability to commercialize a product or any future product candidates and if we fail to comply with FDA regulations and requirements, the FDA could potentially take a number of enforcement actions against us, including the issuance of untitled letters, warning letters, preventing the introduction or delivery of the product into interstate commerce in the US, misbranding charges, product seizures, injunctions, and civil monetary penalties, which would materially and adversely affect our business and financial condition and may cause the price of our securities to fall.

The risks identified in this risk factor relating to regulatory actions and oversight by agencies in the US and throughout the world also apply to the commercialization of any partnered products by our collaboration partners and those commercializing products with respect to which we have an economic interest or right to receive royalties, including GSK, and such regulatory actions and oversight may limit those parties' ability to commercialize such products, which could materially and adversely affect our business and financial condition, and which may cause the price of our securities to fall.

We and/or our collaboration partners and those commercializing products with respect to which we have an economic interest or right to receive royalties may face competition from companies seeking to market generic versions of any approved products in which we have an interest, such as TRELEGY or YUPELRI.

Under the Drug Price Competition and Patent Term Restoration Act of 1984, a company may submit an abbreviated new drug application ("ANDA") under section 505(j) of the Federal Food, Drug, and Cosmetic Act to market a generic version of an approved drug. Because a generic applicant does not conduct its own clinical studies, but instead relies on the FDA's finding of safety and effectiveness for the approved drug, it is able to introduce a competing product into the market at a cost significantly below that of the original drug. Although we have multiple patents protecting YUPELRI until at least 2025 that are listed in the FDA's Approved Drug Products with Therapeutic Equivalence Evaluations, commonly known as the Orange Book, and those commercializing products with respect to which we have an economic interest or right to receive royalties similarly have patents protecting their products, such as TRELEGY and VIBATIV, generic applicants could potentially submit "paragraph IV certifications" to FDA stating that such patents are invalid or will not be infringed by the applicant's product. We have not received any such paragraph IV notifications nor are we aware of any with respect to products in which we have an economic interest or right to receive royalties, but if any competitors successfully challenge the patents related to these products, we and/or our collaboration partners and those commercializing products with respect to which we have an economic interest or right to receive royalties would face substantial competition. If we are not able to compete effectively against such future competition, our business will not grow, our financial condition and operations will suffer and the price of our securities could fall.

For additional discussion of the risk of generic competition to YUPELRI, please see the following risk factor below "*If our efforts to protect the proprietary nature of the intellectual property related to our technologies are not adequate, we may not be able to compete effectively in our current or future markets.*"

We may be treated as a US corporation for US federal income tax purposes.

For US federal income tax purposes, a corporation generally is considered tax resident in the place of its incorporation. Theravance Biopharma is incorporated under Cayman Islands law and established tax residency in Ireland effective July 1, 2015. Therefore, it should be a non-US corporation under this general rule. However, Section 7874 of the Internal Revenue Code of 1986, as amended (the "Code"), contains rules that may result in a foreign corporation being treated as a US corporation for US federal income tax purposes. The application of these rules is complex and there is little guidance regarding certain aspects of their application.

Under Section 7874 of the Code, a corporation created or organized outside the US will be treated as a US corporation for US federal tax purposes if (i) the foreign corporation directly or indirectly acquires substantially all of the properties held directly or indirectly by a US corporation, (ii) the former shareholders of the acquired US corporation hold at least 80% of the vote or value of the shares of the foreign acquiring corporation by reason of holding stock in the US acquired corporation, and (iii) the foreign corporation's "expanded affiliated group" does not have "substantial business activities" in the foreign corporation's country of incorporation relative to its expanded affiliated group's worldwide activities. For this purpose, "expanded affiliated group" generally means the foreign corporation and all subsidiaries in which the foreign corporation, directly or indirectly, owns more than 50% of the stock by vote and value, and "substantial business activities" generally means at least 25% of employees (by number and compensation), assets and gross income of our expanded affiliated group are based, located and derived, respectively, in the country of incorporation.

We do not expect to be treated as a US corporation under Section 7874 of the Code, because we do not believe that the assets contributed to us by Innoviva constituted "substantially all" of the properties of Innoviva (as determined on both a gross and net fair market value basis). However, the Internal Revenue Service may disagree with our conclusion on this point and assert that, in its view, the assets contributed to us by Innoviva did constitute "substantially all" of the properties of Innoviva. In addition, there could be legislative proposals to expand the scope of US corporate tax residence and there could be changes to Section 7874 of the Code or the Treasury Regulations promulgated thereunder that could apply retroactively and could result in Theravance Biopharma being treated as a US corporation.

If it were determined that we should be treated as a US corporation for US federal income tax purposes, we could be liable for substantial additional US federal income tax on our post-Spin-Off taxable income. In addition, though

we have no current plans to pay any dividends, payments of any dividends to non-US holders may be subject to US withholding tax.

Future tax reform, including changes in tax rates and imposition of new taxes, could impact our results of operations and financial condition.

We are incorporated in the Cayman Islands, maintain subsidiaries in the Cayman Islands (until December 2020), the US, the UK and Ireland, and effective July 1, 2015, we migrated our tax residency from the Cayman Islands to Ireland. We are subject to new, evolving or revised tax laws and regulations in such jurisdictions, and the enactment of or increases in taxes, or other changes in the application of existing taxes, in such jurisdictions may have an adverse effect on our business or on our results of operations. Due to economic and political conditions, tax rates in various jurisdictions may be subject to significant change. Our future effective tax rate could be affected by changes in our mix of earnings in countries with differing statutory tax rates, changes in valuation of our deferred tax assets and liabilities, or changes in tax laws or their interpretation, including possible US tax reform and contemplated changes in other countries of long-standing tax principles. These and other similar changes, if finalized and adopted, could have a material impact on our income tax expense and deferred tax balances.

Taxing authorities may challenge our structure and transfer pricing arrangements.

We are incorporated in the Cayman Islands, maintain subsidiaries in the Cayman Islands (until December 2020), the US, the UK and Ireland, and effective July 1, 2015, we migrated our tax residency from the Cayman Islands to Ireland. Due to economic and political conditions, various countries are actively considering changes to existing tax laws. We cannot predict the form or timing of potential legislative changes that could have a material adverse impact on our results of operations. We are aware that Ireland has implemented certain tax law changes, and is expected to implement additional tax law changes, some of which are to comply with the European Union Anti-Tax Avoidance Directives. We are aware that Ireland will implement further tax law changes to comply with the Anti-Tax Avoidance Directives to include reverse-hybrid mismatch and interest limitation rules. We will evaluate and monitor the applicability of these rules to our operations as and when they are enacted.

In April 2020, we became aware of a withholding tax regulation that could be interpreted to apply to certain of our previous intra-group transactions. Additional draft guidance on this withholding tax regime was released in late 2020 and early 2021, and based on our analysis of this guidance, we do not believe the exposure to be material. We continue to monitor the evolving legislation relating to this matter and will consider its impact on our consolidated financial statements.

In addition, significant judgment is required in determining our worldwide provision for income taxes. Various factors may have favorable or unfavorable effects on our income tax rate including, but not limited to the performance of certain functions and ownership of certain assets in tax-efficient jurisdictions such as the Cayman Islands and Ireland, together with intra-group transfer pricing agreements. Taxing authorities may challenge our structure and transfer pricing arrangements through an audit or lawsuit. Responding to or defending such a challenge could be expensive and consume time and other resources, and divert management's time and focus from operating our business. We cannot predict whether taxing authorities will conduct an audit or file a lawsuit challenging this structure, the cost involved in responding to any such audit or lawsuit, or the outcome. We may be required to pay taxes for prior periods, interest, fines or penalties, and may be obligated to pay increased taxes in the future which could result in reduced cash flows and have a material adverse effect on our business, financial condition and growth prospects.

We were a passive foreign investment company, or "PFIC," for 2014, but we were not a PFIC from 2015 through 2021, and we do not expect to be a PFIC for the foreseeable future.

For US federal income tax purposes, we generally would be classified as a PFIC for any taxable year if either (i) 75% or more of our gross income (including gross income of certain 25% or more owned corporate subsidiaries) is "passive income" (as defined for such purposes) or (ii) the average percentage of our assets (including the assets of certain 25% or more owned corporate subsidiaries) that produce passive income or that are held for the production of passive income is at least 50%. In addition, whether our Company will be a PFIC for any taxable year depends on our assets and income over the course of each such taxable year and, as a result, cannot be predicted with certainty until after the end of the year.

Based upon our assets and income during the course of 2014, we believe that our Company and one of our Company's wholly-owned subsidiaries, Theravance Biopharma R&D, Inc. was a PFIC for 2014. Based upon our assets and income from 2015 through 2021, we do not believe that our Company is a PFIC since 2015. Based on existing tax law, we do not expect to be a PFIC for the foreseeable future based on our current business plans and current business model. For any taxable year (or portion thereof) in which our Company is a PFIC that is included in the holding period of a US holder, the US holder is generally subject to additional US federal income taxes plus an interest charge with respect to certain distributions from Theravance Biopharma or gain recognized on a sale of Theravance Biopharma shares. Similar rules would apply with respect to distributions from or gain recognized on an indirect sale of Theravance Biopharma Ireland Limited. US holders of our ordinary shares may have filed an election with respect to Company shares held at any time during 2014 to be treated as owning an interest in a "qualified electing fund" ("QEF") or to "mark to market" their ordinary shares to avoid the otherwise applicable interest charge consequences of PFIC treatment with respect to our ordinary shares. A foreign corporation will not be treated as a QEF for any taxable year in which such foreign corporation is not treated as a PFIC. QEF and mark to market elections generally apply to the taxable year for which the election is made and all subsequent taxable years unless the election is revoked with consent of the Secretary of Treasury. US holders of our ordinary shares should consult their tax advisers regarding the tax reporting implications with respect to any QEF and mark to market elections made with respect to our Company and with respect to their indirect interests in Theravance Biopharma R&D, Inc.

If we are unable to maintain effective internal controls, our business, financial position and results of operations could be adversely affected.

If we are unable to maintain effective internal controls, our business, financial position and results of operations could be adversely affected. We are subject to the reporting and other obligations under the Exchange Act, including the requirements of Section 404 of the Sarbanes-Oxley Act of 2002, which require annual management assessments of the effectiveness of our internal control over financial reporting. Our management is responsible for establishing and maintaining adequate internal control over financial reporting as defined in Rules 13a-15(f) under the Exchange Act. Our internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with accounting principles generally accepted in the US. Any failure to achieve and maintain effective internal controls could have an adverse effect on our business, financial position and results of operations. In addition, our independent registered public accounting firm is required to attest to the effectiveness of our internal control over financial reporting annually. If our independent registered public accounting firm is unable to attest to the effectiveness of our internal control over financial reporting, investor confidence in our reported results will be harmed and the price of our securities may fall. These reporting and other obligations place significant demands on our management and administrative and operational resources, including accounting resources.

Agreements entered into with or for the benefit of GSK in connection with the Spin-Off may significantly restrict our business and affairs.

On March 3, 2014, in connection with the Spin-Off, we, Innoviva and GSK entered into a number of agreements that may significantly restrict our business and affairs. In particular, we, Innoviva and GSK entered into the Master Agreement which, among other things, requires GSK's consent to make any changes to (i) a Separation and Distribution Agreement and ancillary agreements that would, individually or in the aggregate, reasonably be expected to adversely affect GSK in any material respect or (ii) the TRC LLC Agreement, which consent is not to be unreasonably withheld, conditioned or delayed, provided that GSK may withhold, condition or delay such consent in its sole discretion with respect to certain sections of the TRC LLC Agreement and any changes to the governance structure of TRC, the confidentiality restrictions, the consent rights, and the transfer restrictions in the TRC LLC Agreement. We and GSK also entered into (i) the Governance Agreement that expired on December 31, 2017, (ii) a registration rights agreement that gives GSK certain registration rights with respect to our ordinary shares held by GSK and (iii) an extension agreement that extends to us certain restrictive covenants similar to those applicable to Innoviva under the GSK Agreements. There can be no assurance that these restrictions will not materially harm our business, particularly given that GSK's interests may not be aligned with the interests of our business or our other shareholders.

Certain of our directors and officers may have actual or potential conflicts of interest because of their equity ownership in Innoviva, which actual or potential conflicts may harm our business, prospects and financial condition and result in the diversion of corporate opportunities to Innoviva.

Certain of our directors and officers hold shares of Innoviva's common stock or rights to acquire such shares, and these holdings may be significant for some of these individuals compared to their total assets. This ownership of Innoviva common stock by certain of our directors and officers may create, or may create the appearance of, conflicts of interest when these directors and officers are faced with decisions that could have different implications for Innoviva and for us. For example, potential or actual conflicts could arise relating to: our relationship with Innoviva, including Innoviva's and our respective rights and obligations under agreements entered into in connection with the Spin-Off; Innoviva's management of TRC, particularly given that we and Innoviva have different economic interests in TRC; and corporate opportunities that may be available to both companies in the future. Although we and Innoviva have implemented policies and procedures to identify and properly address such potential and actual conflicts of interest, there can be no assurance that, when such conflicts are resolved in accordance with applicable laws, such conflicts of interest will not harm our business, prospects and financial condition and result in the diversion of corporate opportunities to Innoviva.

If we are required to indemnify Innoviva or Cumberland, or if we are not able to enforce our indemnification rights against Innoviva or Cumberland, our business prospects and financial condition may be harmed.

We agreed to indemnify Innoviva from and after the Spin-Off with respect to (i) all debts, liabilities and obligations transferred to us in connection with the Spin-Off (including our failure to pay, perform or otherwise promptly discharge any such debts, liabilities or obligations after the Spin-Off), (ii) any misstatement or omission of a material fact resulting in a misleading statement in our Information Statement distributed to Innoviva stockholders in connection with the Spin-Off and (iii) any breach by us of certain agreements entered into with Innoviva in connection with the Spin-Off (namely, the Separation and Distribution Agreement, a Transition Services Agreement, an Employee Matters Agreement, a Tax Matters Agreement, and a Facility Sublease Agreement). We are not aware of any existing indemnification obligations at this time, but any such indemnification obligations that may arise could be significant. Under the terms of the Separation and Distribution Agreement, Innoviva agreed to indemnify us from and after the Spin-Off with respect to (i) all debts, liabilities and obligations retained by Innoviva after the Spin-Off (including its failure to pay, perform or otherwise promptly discharge any such debts, liabilities or obligations after the Spin-Off) and (ii) any breach by Innoviva of the Separation and Distribution Agreement, the Transition Services Agreement, the Employee Matters Agreement, the Tax Matters Agreement, and the Facility Sublease Agreement. Our and Innoviva's ability to satisfy these indemnities, if called upon to do so, will depend upon our and Innoviva's future financial strength. If we are required to indemnify Innoviva, or if we are not able to enforce our indemnification rights against Innoviva, our business prospects and financial condition may be harmed.

In addition, the agreement relating to the sale of VIBATIV to Cumberland Pharmaceuticals Inc. ("Cumberland") contains indemnification obligations of both us and Cumberland. If we are required to indemnify Cumberland or if we are unable to enforce our indemnification rights against Cumberland for any reason, our business and financial condition may be harmed.

RISKS RELATED TO LEGAL AND REGULATORY UNCERTAINTY

If our efforts to protect the proprietary nature of the intellectual property related to our technologies are not adequate, we may not be able to compete effectively in our current or future markets.

We rely upon a combination of patents, patent applications, trade secret protection and confidentiality agreements to protect the intellectual property related to our technologies. Any involuntary disclosure to or misappropriation by third parties of this proprietary information could enable competitors to quickly duplicate or surpass our technological achievements, thus eroding our competitive position in our market. The status of patents in the biotechnology and pharmaceutical field involves complex legal and scientific questions and is very uncertain. As of December 31, 2021, we owned 285 issued US patents and 1,968 granted foreign patents, as well as additional pending US and foreign patent applications. Our patent applications may be challenged or fail to result in issued patents and our existing or future patents may be invalidated or be too narrow to prevent third parties from developing or designing around these patents. If the sufficiency of the breadth or strength of protection provided by our patents with respect to a

product candidate is threatened, it could dissuade companies from collaborating with us to develop product candidates and threaten our ability to commercialize products. Further, if we encounter delays in our clinical trials or in obtaining regulatory approval of our product candidates, the patent lives of the related product candidates would be reduced.

In addition, we rely on trade secret protection and confidentiality agreements to protect proprietary know-how that is not patentable, for processes for which patents are difficult to enforce and for any other elements of our drug discovery and development processes that involve proprietary know-how, information and technology that is not covered by patent applications. Although we require our employees, consultants, advisors and any third parties who have access to our proprietary know-how, information and technology to enter into confidentiality agreements, we cannot be certain that this know-how, information and technology will not be misappropriated, disclosed or used for unauthorized purposes or that competitors will not otherwise gain access to our trade secrets or independently develop substantially equivalent information and techniques. Further, the laws of some foreign countries do not protect proprietary rights to the same extent as the laws of the US. As a result, we may encounter significant problems in protecting and defending our intellectual property both in the US and abroad. If we are unable to prevent material disclosure of the intellectual property related to our technologies to third parties, we will not be able to establish or, if established, maintain a competitive advantage in our market, which could materially adversely affect our business, financial condition and results of operations, which could cause the price of our securities to fall.

Litigation to protect or defend our intellectual property or third-party claims of intellectual property infringement would require us to divert resources and may prevent or delay our drug discovery and development efforts.

Our commercial success depends in part on us and our partners not infringing the patents and proprietary rights of third parties. Third parties may assert that we or our partners are using their proprietary rights without authorization. There are third-party patents that may cover materials or methods for treatment related to our product candidates. At present, we are not aware of any patent infringement claims with merit that would adversely and materially affect our ability to develop our product candidates, but nevertheless the possibility of third-party allegations cannot be ruled out. In addition, third parties may obtain patents in the future and claim that use of our technologies infringes upon these patents. Furthermore, parties making claims against us or our partners may obtain injunctive or other equitable relief, which could effectively block our ability to further develop and commercialize one or more of our product candidates. Defense against these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee resources from our business.

In the event of a successful claim of infringement against us, we may have to pay substantial damages, obtain one or more licenses from third parties or pay royalties. In addition, even in the absence of litigation, we may need to obtain licenses from third parties to advance our research or allow commercialization of our product candidates, and we have done so from time to time. We may fail to obtain any of these licenses at a reasonable cost or on reasonable terms, if at all. In that event, we would be unable to further develop and commercialize one or more of our product candidates, which could harm our business significantly.

In addition, in the future we could be required to initiate litigation to enforce our proprietary rights against infringement by third parties, prevent the unauthorized use or disclosure of our trade secrets and confidential information, or defend the validity of our patents. For example, in 2017, we filed a lawsuit against a former employee for misappropriation of certain of our confidential, proprietary and trade secret information. While this litigation has since been resolved, prosecution of claims to enforce or defend our rights against others involve substantial litigation expenses and divert substantial employee resources from our business but may not result in adequate remedy to us or sufficiently mitigate the harm to our business caused by any intellectual property infringement, unauthorized access, use or disclosure of trade secrets. If we fail to effectively enforce our proprietary rights against others, our business will be harmed and the price of our securities could fall.

If the efforts of our partners or future partners to protect the proprietary nature of the intellectual property related to collaboration assets are not adequate, the future commercialization of any medicines resulting from collaborations could be delayed or prevented, which would materially harm our business and could cause the price of our securities to fall.

The risks identified in the two preceding risk factors may also apply to the intellectual property protection efforts of our partners or future partners and to GSK with respect to the GSK-Partnered Respiratory Programs in which

we hold an economic interest. To the extent the intellectual property protection of any partnered assets is successfully challenged or encounters problems with the US Patent and Trademark Office or other comparable agencies throughout the world, the future commercialization of these potential medicines could be delayed or prevented. Any challenge to the intellectual property protection of a late-stage development asset, particularly those of the GSK-Partnered Respiratory Programs in which we hold an economic interest, could harm our business and cause the price of our securities to fall.

Product liability and other lawsuits could divert our resources, result in substantial liabilities and reduce the commercial potential of our medicines.

The risk that we may be sued on product liability claims is inherent in the development and commercialization of pharmaceutical products. Side effects of, or manufacturing defects in, products that we or our partners develop or commercialize could result in the deterioration of a patient's condition, injury or even death. Once a product is approved for sale and commercialized, the likelihood of product liability lawsuits tends to increase. Claims may be brought by individuals seeking relief for themselves or by individuals or groups seeking to represent a class, asserting injuries based both on potential adverse effects described in the label as well as adverse events not yet observed. We also face an inherent risk of product liability exposure related to the testing of our product candidates in human clinical trials. In addition, changes in laws outside the US are expanding our potential liability for injuries that occur during clinical trials. Product liability claims could harm our reputation, regardless of the merit or ultimate success of the claim, which may adversely affect our and our partners' ability to commercialize our products and cause the price of our securities to fall. These lawsuits may divert our management from pursuing our business strategy and may be costly to defend. In addition, if we are held liable in any of these lawsuits, we may incur substantial liabilities and may be forced to limit or forgo further commercialization of the applicable products.

Although we maintain general liability and product liability insurance, this insurance may not fully cover potential liabilities and we cannot be sure that our insurer will not disclaim coverage as to a future claim. In addition, inability to obtain or maintain sufficient insurance coverage at an acceptable cost or to otherwise protect against potential product liability claims could prevent or inhibit the commercial production and sale of our products, which could adversely affect our business.

We may also be required to prosecute or defend general commercial, intellectual property, securities and other lawsuits. Litigation typically involves substantial expenses and diverts substantial employee resources from our business. The cost of defending any product liability litigation or engaging in any other legal proceeding, even if resolved in our favor, could be substantial and uncertainties resulting from the initiation and continuation of the litigation or other proceedings could have a material adverse effect on our ability to compete in the marketplace and achieve our business goals.

If we fail to comply with data protection laws and regulations, we could be subject to government enforcement actions (which could include civil or criminal penalties), private litigation and/or adverse publicity, which could negatively affect our operating results and business.

We are subject to data protection laws and regulations (i.e., laws and regulations that address privacy and data security). In the US, numerous federal and state laws and regulations, including state data breach notification laws, state health information and/or genetic privacy laws, and federal and state consumer protection laws (e.g., Section 5 of the FTC Act), govern the collection, use, disclosure, and protection of health related and other personal information. In California, the California Consumer Privacy Act ("CCPA") took effect on January 1, 2020. The CCPA establishes certain requirements for data use and sharing transparency, and provides California residents certain rights concerning the use, disclosure, and retention of their personal data. In addition, in November 2020, California voters approved the California Privacy Rights Act ("CPRA") ballot initiative which introduced significant amendments to the CCPA and established and funded a dedicated California privacy regulator, the California Privacy Protection Agency ("CPPA"). The amendments introduced by the CPRA go into effect on January 1, 2023, and new implementing regulations are expected to be introduced by the CPPA. And in 2021, Virginia and Colorado adopted laws, effective January 1, 2023, and July 1, 2023, respectively, introducing new privacy obligations for which we may need to take additional steps to comply. Similarly, there are a number of legislative proposals and enactments in the United States, at both the federal and state level, that could impose new obligations or limitations in areas affecting our business. These laws and regulations are evolving and subject to interpretation, and may impose limitations on our activities or otherwise adversely affect our business. The obligations to comply with the CCPA and evolving legislation involve, among other

things, updates to our notices and the development of new processes internally and with our partners. We may be subject to fines, penalties, or private actions in the event of non-compliance with such laws.

In addition, we may obtain health information from third parties (e.g., healthcare providers who prescribe our products) that are subject to privacy and security requirements under the Health Insurance Portability and Accountability Act of 1996, the Health Information Technology for Economic and Clinical Health Act, and their implementing regulations, (collectively, "HIPAA"). Although we are not directly subject to HIPAA we could be subject to criminal penalties if we knowingly obtain, use, or disclose individually identifiable health information maintained by a HIPAA covered entity in a manner that is not authorized or permitted by HIPAA. HIPAA generally requires that healthcare providers and other covered entities obtain written authorizations from patients prior to disclosing protected health information of the patient (unless an exception to the authorization requirement applies). If authorization is required and the patient fails to execute an authorization or the authorization fails to contain all required provisions, then we may not be allowed access to and use of the patient's information and our research efforts could be impaired or delayed. Furthermore, use and disclosure of protected health information that is provided to us pursuant to a valid patient authorization is subject to the limits set forth in the authorization (e.g., for use in research and in submissions to regulatory authorities for product approvals). Moreover, patients about whom we or our partners obtain information, as well as the providers who share this information with us, may have contractual rights that limit our ability to use and disclose the information. In addition, HIPAA does not replace federal, state, international or other laws that may grant individuals even greater privacy protections.

EU Member States and other jurisdictions where we operate have adopted data protection laws and regulations, which impose significant compliance obligations. For example, the General Data Protection Regulation ("GDPR") which became applicable on May 25, 2018, replacing the EU Data Protection Directive, imposes strict obligations and restrictions on the ability to collect, analyze and transfer personal data, including health data from clinical trials and adverse event reporting.

Switzerland has adopted laws that impose restrictions and obligations similar to the GDPR. The obligations and restrictions under the GDPR and Switzerland's laws concern, in particular, in some instances the consent of the individuals to whom the personal data relate, the information provided to the individuals, the transfer of personal data out of the European Economic Area ("EEA") or Switzerland, security breach notifications, security and confidentiality of the personal data, as well as substantial potential fines, in some cases up to 4% of global revenues, for breaches of the data protection obligations. Data protection authorities from the different EU Member States and the EEA may interpret the GDPR and applicable related national laws differently which could effectively result in requirements additional to those currently understood to apply under the GDPR. In addition, guidance on implementation and compliance practices may be updated or otherwise revised, which adds to the complexity of processing personal data in the EU. When processing personal data of subjects in the EU, we have to comply with applicable data protection and electronic communications laws. In particular, as we rely on service providers processing personal data of subjects in the EU, we have to enter into suitable contract terms with such providers and receive sufficient guarantees that such providers meet the requirements of the applicable data protection laws, particularly the GDPR which imposes specific and relevant obligations.

Legal mechanisms to allow for the transfer of personal data from the EEA to the US have been challenged in the European Court of Justice, which generally increases uncertainty around compliance with EU privacy law requirements as these relate to transfer of data from the EU to the US. In 2016, the European Commission and the US Department of Commerce ("DOC") put in place the EU US "Privacy Shield," which has been relied on by some US companies since that time to transfer data to the US. However, on July 16, 2020, the European Court of Justice ruled that the Privacy Shield is invalid. As a result, from July 16, 2020 companies could no longer rely on the Privacy Shield as a basis on which to transfer personal data from the EU to the US. Data exporters and US-based companies are permitted to rely on other authorized means and procedures to transfer personal data subject to the GDPR to the US. Recent changes have been made to another commonly used authorized procedure to transfer personal data out of the EU, the European Commission's Standard Contractual Clauses (SCCs). In June 2021, the European Commission published updated versions of the SCCs, which, if companies are relying on them as the mechanism to transfer personal information from the EEA to the US (or to other jurisdictions not recognized as adequate by the EU), must be incorporated into new and existing agreements within prescribed timeframes. The UK is expected to publish final versions of their own SCCs during 2022. Updating agreements to incorporate these new SCCs for the EEA and UK may require significant time and

resources to implement, including through adjusting our operations, conducting requisite data transfer assessments, and revising our contracts. Companies that have not taken steps to demonstrate that their SCCs and personal data recipients in the US or other non-adequate jurisdictions are suitable to receive the personal data may be subject to enforcement actions by competent authorities in the EU for failure to comply with related data privacy rules.

If we or our vendors fail to comply with applicable data privacy laws concerning, or if the legal mechanisms we or our vendors rely upon to allow, the transfer of personal data from the EEA or Switzerland to the US (or other countries not considered by the European Commission to provide an adequate level of data protection) are not considered adequate, we could be subject to government enforcement actions, including an order to stop transferring the personal data outside of the EEA and significant penalties against us. Moreover, our business could be adversely impacted if our ability to transfer personal data out of the EEA or Switzerland to the US is restricted, which could adversely impact our operating results.

Failure to comply with data protection laws and regulations could result in unfavorable outcomes, including increased compliance costs, delays or impediments in the development of new products, increased operating costs, diversion of management time and attention, government enforcement actions and create liability for us (which could include civil, administrative, and/or criminal penalties), private litigation and/or adverse publicity that could negatively affect our operating results and business.

Changes in healthcare law and implementing regulations, including government restrictions on pricing and reimbursement, as well as healthcare policy and other healthcare payor cost-containment initiatives, may negatively impact us, our collaboration partners, or those commercializing products with respect to which we have an economic interest or right to receive royalties.

The continuing efforts of the government, insurance companies, managed care organizations and other payors of health care costs to contain or reduce costs of health care may adversely affect us, our collaboration partners, or those commercializing products with respect to which we have an economic interest or right to receive royalties in regard to one or more of the following:

- the ability to set and collect a price believed to be reasonable for products;
- the ability to generate revenues and achieve profitability; and
- the availability of capital.

The pricing and reimbursement environment for products may change in the future and become more challenging due to, among other reasons, policies advanced by the presidential administration, federal agencies, new healthcare legislation passed by Congress or fiscal challenges faced by all levels of government health administration authorities. Among policy makers and payors in the US and elsewhere, there is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality and expanding access to healthcare. In the US, the pharmaceutical industry has been a particular focus of these efforts and has been and may in the future be significantly affected by major regulatory or legislative initiatives, including those related to pricing of or reimbursement for prescription drugs. We expect we, our collaboration partners or those commercializing products with respect to which we have an economic interest or right to receive royalties may experience pricing pressures in connection with the sale of drug products, due to the trend toward managed healthcare, the increasing influence of health maintenance organizations and additional legislative enactments and administrative policies.

The Patient Protection and Affordable Care Act, as amended (the “Healthcare Reform Act”), is a sweeping measure intended to expand healthcare coverage within the US, primarily through the imposition of health insurance mandates on employers and individuals (the latter of which since made non-enforceable), the provision of subsidies to eligible individuals enrolled in plans offered on the health insurance exchanges, and expansion of the Medicaid program. This law has substantially changed the way healthcare is financed by both governmental and private insurers and has significantly impacted the pharmaceutical industry. The Healthcare Reform Act contains a number of provisions that impact our business and operations, including those governing enrollment in federal healthcare programs, reimbursement changes, benefits for patients within a coverage gap in the Medicare Part D prescription drug program (commonly

known as the “donut hole”), rules regarding prescription drug benefits under the health insurance exchanges, changes to the Medicare Drug Rebate program, expansion of the Public Health Service Act’s 340B drug pricing program, fraud and abuse and enforcement. These changes have impacted previously existing government healthcare programs and have resulted in the development of new programs, including Medicare payment for performance initiatives and improvements to the physician quality reporting system and feedback program.

Congress could enact additional legislation that further increases Medicaid drug rebates or other costs and charges associated with participating in the Medicaid Drug Rebate program or other government programs. For example, Congress is considering Medicare Part B inflation rebate, under which manufacturers would owe additional rebates if the average sales price of a drug were to increase faster than the pace of inflation. Congress also could enact a drug price negotiation program under which the prices for certain high Medicare spend single source drugs would be capped by reference to the non-federal average manufacturer price. These or any other legislative changes could impact the market conditions for our products. We further expect continued scrutiny on government price reporting from Congress, agencies, and other bodies.

On December 21, 2020, CMS issued a final regulation that modified prior Medicaid Drug Rebate program regulations to permit reporting multiple best price figures with regard to value-based purchasing arrangements (beginning in 2022); provide definitions for “line extension,” “new formulation,” and related terms, with the practical effect of expanding the scope of drugs considered to be line extensions that are subject to an alternative rebate formula (beginning in 2022); and revise best price and average manufacturer price exclusions of manufacturer-sponsored patient benefit programs, specifically regarding applicability of such exclusions in the context of pharmacy benefit manager “accumulator” programs (beginning in 2023). The issuance of regulations and coverage expansion by various governmental agencies relating to the Medicaid Drug Rebate program has increased and will continue to increase the costs and the complexity of compliance, has been and will be time-consuming to implement, and could have a material adverse effect on results of operations for us, our collaboration partners, or those commercializing products with respect to which we have an economic interest or right to receive royalties, particularly if CMS challenges the approach taken in the implementation of the final regulations.

Certain provisions of the Healthcare Reform Act have been subject to judicial challenges as well as efforts to modify them or to alter their interpretation or implementation. For example, the Tax Cuts and Jobs Act enacted on December 22, 2017 (the “Tax Act”), eliminated the shared responsibility payment for individuals who fail to maintain minimum essential coverage under section 5000A of the Internal Revenue Code of 1986, commonly referred to as the individual mandate, effective January 1, 2019. Additional legislative changes to and regulatory changes under the Healthcare Reform Act remain possible, but the nature and extent of such potential additional changes are uncertain at this time. We expect that the Healthcare Reform Act, its implementation, efforts to modify, or invalidate the Healthcare Reform Act, or portions thereof, or its implementation, and other healthcare reform measures that may be adopted in the future, could have a material adverse effect on our industry generally and on the ability of us, our collaboration partners, or those commercializing products with respect to which we have an economic interest or right to receive royalties to maintain or increase sales of existing products or to successfully commercialize product candidates, if approved.

The Bipartisan Budget Act of 2018, among other things, amended the Healthcare Reform Act to increase the point-of-sale discounts that manufacturers must agree to offer under the Medicare Part D coverage discount program from 50% to 70% off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer’s outpatient drugs to be covered under Medicare Part D. Civil monetary penalties can be applied if a manufacturer fails to provide these discounts in the amount of 125 percent of the discount that was due. Congress could enact legislation that sunsets this discount program and replaces it with a new manufacturer discount program. Congress further could enact a Medicare Part D inflation rebate, under which manufacturers would owe additional rebates if the average manufacturer price of a drug were to increase faster than the pace of inflation.

Additionally, in November 2020, the US Department of Health and Human Services finalized a previously abandoned proposal to amend the discount safe harbor regulation of the federal anti-kickback statute in a purported effort to create incentives to manufacturers to lower their list prices, and to lower federal program beneficiary out-of-pocket costs. The rule, for which the effective date was delayed to 2026 in the 2021 Infrastructure Investment and Jobs

Act, revises the discount safe harbor to exclude manufacturer rebates to Medicare Part D plans, either directly or through pharmacy benefit managers ("PBMs"), creates a new safe harbor for point-of-sale price reductions that are set in advance and are available to the beneficiary at the point-of-sale, and creates a new safe harbor for service fees paid by manufacturers to PBMs for services rendered to the manufacturer. It is unclear whether the rule will be further delayed, rewritten, or allowed to go into effect, and if so, what the effect of the rule will be on negotiations of coverage for our products with Medicare Part D plans, or whether the rule will affect our coverage arrangements with commercial insurers. It is also unclear whether the rule will have the intended effect of reducing net prices and beneficiary out-of-pocket costs without also increasing Medicare Part D premiums, which may impact the willingness of Part D plans to cover our products and the price concessions or other terms the plans or their PBMs may seek from us. There have been other proposals to modify the Medicare Part D benefit, including by imposing federally mandated rebates on all drugs dispensed to Medicare Part D enrollees or on only those drugs dispensed to certain groups of lower income beneficiaries. If any of these proposals are adopted including any that result in additional rebates, this could have a negative impact on revenues for our collaboration partners, or those commercializing products with respect to which we have an economic interest or right to receive royalties, which could impact our revenues.

On August 2, 2011, the Budget Control Act of 2011, among other things, created the Joint Select Committee on Deficit Reduction to recommend to Congress proposals for spending reductions. The Joint Select Committee did not achieve a targeted deficit reduction, which triggered the legislation's automatic reductions. In concert with subsequent legislation, this has resulted in aggregate reductions to Medicare payments to providers of, on average, 2% per fiscal year through 2030 (with the exception of a temporary suspension from May 1, 2020 through May 31, 2022, due to the COVID-19 pandemic). The law provides for 1% Medicare sequestration in the second quarter of 2022 and allows the full 2% sequestration thereafter until 2030. To offset the temporary suspension during the COVID-19 pandemic, in 2030, the sequestration will be 2.25% for the first half of the year, and 3% in the second half of the year. As long as these cuts remain in effect, they could adversely impact payment for any products that are reimbursed under Medicare.

Individual states in the United States have also increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement limitations, marketing cost disclosure and transparency measures, and, in some cases, measures designed to encourage importation from other countries and bulk purchasing. For example, California has enacted a prescription drug price transparency law requiring prescription drug manufacturers to provide advance notice and explanation for price increases of certain drugs with prices that exceed a specified threshold, and to report new prescription drugs introduced to the market at a wholesale acquisition cost exceeding the Medicare Part D specialty drug threshold.

We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for product or additional pricing pressures for our collaboration partners, or those commercializing products with respect to which we have an economic interest or right to receive royalties, which could impact our revenues.

If we failed to comply with our reporting and payment obligations under the Medicaid Drug Rebate program or other governmental pricing programs, we could be subject to additional reimbursement requirements, penalties, sanctions and fines, which could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

Prior to the sale of VIBATIV to Cumberland, we had certain price reporting obligations to the Medicaid Drug Rebate program and other governmental pricing programs, and we had obligations to report average sales price under the Medicare program. Following the consummation of the transaction with Cumberland, our price reporting obligations related to VIBATIV have been transitioned to Cumberland, and price reporting obligations for YUPELRI reside with Viatris. We retain certain obligations with respect to record retention for these programs.

Under the Medicaid Drug Rebate program, a manufacturer is required to pay a rebate to each state Medicaid program for its covered outpatient drugs that are dispensed to Medicaid beneficiaries and paid for by a state Medicaid program as a condition of having federal funds being made available to the states for our drugs under Medicaid and Medicare Part B. Those rebates are based on pricing data reported by the manufacturer on a monthly and quarterly basis to CMS, the federal agency that administers the Medicaid Drug Rebate program. These data include the average

manufacturer price and, in the case of innovator products, the best price for each drug which, in general, represents the lowest price available from the manufacturer to any entity in the US in any pricing structure, calculated to include all sales and associated rebates, discounts and other price concessions. The amount of the rebate is adjusted upward if the average manufacturer price increases at a pace faster than inflation (measured by reference to the Consumer Price Index - Urban). Currently, the rebate is capped at 100 percent of the average manufacturer price, but, effective January 1, 2024, this cap on the rebate will be removed, and our rebate liability could increase accordingly.

Federal law requires that any company that participates in the Medicaid Drug Rebate program also participate in the Public Health Service's 340B drug pricing program in order for federal funds to be available for the manufacturer's drugs under Medicaid and Medicare Part B. The 340B program requires participating manufacturers to agree to charge no more than the 340B "ceiling price" for the manufacturer's covered outpatient drugs to a variety of community health clinics and other entities that receive health services grants from the Public Health Service, as well as hospitals that serve a disproportionate share of low-income patients. Manufacturers also are required to report their 340B ceiling prices to HRSA on a quarterly basis, and HRSA then publishes them to 340B covered entities. A final regulation regarding the calculation of the 340B ceiling price and the imposition of civil monetary penalties on manufacturers that knowingly and intentionally overcharge covered entities became effective on January 1, 2019. Moreover, under a final regulation effective January 13, 2021, HRSA newly established an administrative dispute resolution ("ADR") process for claims by covered entities that a manufacturer has engaged in overcharging, and by manufacturers that a covered entity violated the prohibitions against diversion or duplicate discounts. Such claims are to be resolved through an ADR panel of government officials rendering a decision that could be appealed only in federal court. An ADR proceeding could subject us to onerous procedural requirements and could result in additional liability.

Federal law also requires that manufacturers report average sales price information for certain categories of drugs that are paid under the Medicare Part B program to CMS on a quarterly basis. Manufacturers calculate the average sales price based on a statutorily defined formula as well as regulations and interpretations of the statute by CMS. CMS uses these submissions to determine payment rates for drugs under Medicare Part B. Effective January 1, 2023, manufacturers will be obligated to pay refunds to Medicare for single source drugs or biologicals, or biosimilar biological products, reimbursed under Medicare Part B and packaged in single-dose containers or single-use packages, for units of discarded drug reimbursed by Medicare Part B in excess of 10 percent of total allowed charges under Medicare Part B for that drug. Manufacturers that fail to pay refunds could be subject to civil monetary penalties of 125 percent of the refund amount.

Pricing and rebate calculations vary across products and programs, are complex, and are often subject to interpretation by the manufacturer, governmental or regulatory agencies and the courts. A manufacturer that becomes aware that its Medicaid reporting for a prior quarter was incorrect, or has changed as a result of recalculation of the pricing data, is obligated to resubmit the corrected data for up to three years after those data originally were due. Such restatements and recalculations increase the costs for complying with the laws and regulations governing the Medicaid Drug Rebate program and could result in an overage or underage in our rebate liability for past quarters. Price recalculations also may affect the 340B ceiling price.

We may be liable for errors associated with our submission of pricing data for VIBATIV for historic periods, and we may retain some liability for price reporting by Cumberland for VIBATIV sold under our labeler code. In addition to retroactive rebates and the potential for 340B program refunds, if we are found to have knowingly submitted any false price information to the government, we may be liable for significant civil monetary penalties per item of false information. If we are found to have made a misrepresentation in the reporting of our average sales price, the Medicare statute provides for significant civil monetary penalties for each misrepresentation for each day in which the misrepresentation was applied. If we are found to have charged 340B covered entities more than the statutorily mandated ceiling price, we could be subject to significant civil monetary penalties and/or such failure also could be grounds for HRSA to terminate a manufacturer's agreement to participate in the 340B program, in which case covered outpatient drugs under our labeler code may no longer be eligible for federal payment under the Medicaid or Medicare Part B program. If we are found to have not submitted required price data on a timely basis, that could result in a significant civil monetary penalty per day for each day the information is late beyond the due date. Such failure also could be grounds for CMS to terminate our Medicaid drug rebate agreement, pursuant to which we participate in the Medicaid program. In the event that CMS terminates our rebate agreement, federal payments may not be available under Medicaid or Medicare Part B for covered outpatient drugs under our labeler code.

In order to be eligible to have its products paid for with federal funds under the Medicaid and Medicare Part B programs and purchased by the Department of Veterans Affairs ("VA"), Department of Defense ("DoD"), Public Health Service, and Coast Guard (the "Big Four agencies") and certain federal grantees, a manufacturer is required to participate in the VA Federal Supply Schedule ("FSS") pricing program, established under Section 603 of the Veterans Health Care Act of 1992. Under this program, the manufacturer is obligated to make its covered drugs available for procurement on an FSS contract and charge a price to the Big Four agencies that is no higher than the Federal Ceiling Price ("FCP"), which is a price calculated pursuant to a statutory formula. The FCP is derived from a calculated price point called the "non-federal average manufacturer price" ("Non-FAMP"), which the manufacturer calculates and reports to the VA on a quarterly and annual basis. Pursuant to applicable law, knowing provision of false information in connection with a Non-FAMP filing can subject a manufacturer to significant penalties for each item of false information. The FSS contract also contains extensive disclosure and certification requirements.

Under Section 703 of the National Defense Authorization Act for FY 2008, the manufacturer is required to pay quarterly rebates to DoD on utilization of its innovator products that are dispensed through DoD's Tricare network pharmacies to Tricare beneficiaries. The rebates are calculated as the difference between the annual Non-FAMP and FCP for the calendar year that the product was dispensed. A manufacturer that overcharges the government in connection with the FSS contract or Tricare Retail Pharmacy Rebate Program, whether due to a misstated FCP or otherwise, is required to refund the difference to the government. Failure to make necessary disclosures and/or to identify contract overcharges can result in allegations against us under the False Claims Act and other laws and regulations.

Individual states in the United States, as noted, have also passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including marketing cost disclosure and transparency measures. Some states require the submission of reports related to pricing information, including based on the introduction of new prescription drugs, certain increases in wholesale acquisition cost of prescription drugs, marketing of prescription drugs within the state, and sales of prescription drugs in or into the state. Some states may pursue available enforcement measures, including imposition of civil monetary penalties, for a manufacturer's failure to report such information.

Our relationships with customers and third-party payors are subject to applicable anti-kickback, fraud and abuse, transparency and other healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties, exclusion, contractual damages, reputational harm and diminished profits and future earnings.

Healthcare providers, physicians, distributors and third-party payors play a primary role in the distribution, recommendation and prescription of any pharmaceutical product for which we obtain marketing approval. Our arrangements with third-party payors and customers expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements through which we market, sell and distribute any products for which we have obtained or may obtain marketing approval. Restrictions under applicable federal and state healthcare laws and regulations include the following:

- The US federal healthcare Anti-Kickback Statute prohibits any person from, among other things, knowingly and willfully offering, paying, soliciting, or receiving remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchasing, leasing, ordering or arranging for or recommending of any good or service for which payment may be made, in whole or in part, under federal and state healthcare programs such as Medicare and Medicaid. The term "remuneration" has been broadly interpreted to include anything of value. The Anti-Kickback Statute is subject to evolving interpretation and has been applied by government enforcement officials to a number of common business arrangements in the pharmaceutical industry. The government can establish a violation of the Anti-Kickback Statute without proving that a person or entity had actual knowledge of the statute or specific intent to violate it. There are a number of statutory exemptions and regulatory safe harbors protecting some common activities from prosecution; however, those exceptions and safe harbors are drawn narrowly. Failure to meet all of the requirements of a particular statutory exception or regulatory safe harbor does not make the conduct per se illegal under the Anti-Kickback Statute, but the legality of the arrangement will be evaluated on a case-by-case basis based on the totality of the facts and circumstances. We seek to comply with the available statutory exemptions and safe harbors whenever possible, but our

practices may not in all cases meet all of the criteria for safe harbor protection from anti-kickback liability. Moreover, there are no safe harbors for many common practices, such as educational and research grants or patient or product assistance programs.

- The federal civil False Claims Act prohibits, among other things, knowingly presenting, or causing to be presented, claims for payment of government funds that are false or fraudulent, or knowingly making, or using or causing to be made or used, a false record or statement material to a false or fraudulent claim to avoid, decrease, or conceal an obligation to pay money to the federal government. Private individuals, commonly known as "whistleblowers," can bring civil False Claims Act *qui tam* actions, on behalf of the government and such individuals and may share in amounts paid by the entity to the government in recovery or settlement. In recent years, several pharmaceutical and other healthcare companies have faced enforcement actions under the federal False Claims Act for, among other things, allegedly submitting false or misleading pricing information to government health care programs and providing free product to customers with the expectation that the customers would bill federal programs for the product. Federal enforcement agencies also have showed increased interest in pharmaceutical companies' product and patient assistance programs, including reimbursement and co-pay support services, and a number of investigations into these programs have resulted in significant civil and criminal settlements. Other companies have faced enforcement actions for causing false claims to be submitted because of the companies' marketing the product for unapproved, and thus non-reimbursable, uses. In addition, a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal civil False Claims Act. False Claims Act liability is potentially significant in the healthcare industry because the statute provides for treble damages and significant mandatory penalties per false claim or statement for violations. Because of the potential for large monetary exposure, healthcare and pharmaceutical companies often resolve allegations without admissions of liability for significant and material amounts to avoid the uncertainty of treble damages and per claim penalties that may be awarded in litigation proceedings. As part of these resolutions, Companies may enter into corporate integrity agreements with the government, which may impose substantial costs on companies to ensure compliance. Criminal penalties, including imprisonment and criminal fines, are also possible for making or presenting a false, fictitious or fraudulent claim to the federal government.

- HIPAA, among other things, imposes criminal and civil liability for knowingly and willfully executing a scheme to defraud any healthcare benefit program, including private third-party payors, and also imposes obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information. HIPAA also prohibits knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement or representation, or making or using any false writing or document knowing the same to contain any materially false fictitious or fraudulent statement or entry in connection with the delivery of or payment for healthcare benefits, items or services. Similar to the federal healthcare Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it to have committed a violation.

- The federal Physician Payment Sunshine Act, implemented as the Open Payments Program, requires certain manufacturers of drugs, devices, biologics, and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program (with certain exceptions) to report annually to the US Department of Health and Human Services, Centers for Medicare and Medicaid Services, information related to payments and other transfers of value, directly or indirectly, to physicians (defined to include doctors, dentists, optometrists, podiatrists, and chiropractors) and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members. Beginning in 2022, applicable manufacturers also will be required to report information regarding payments and transfers of value provided to physician assistants, nurse practitioners, clinical nurse specialists, certified nurse anesthetists, and certified nurse-midwives. A manufacturer's failure to submit timely, accurately and completely the required information for all payments, transfers of value or ownership or investment interests may result in civil monetary penalties.

- Analogous state laws and regulations, such as state anti-kickback and false claims laws, may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by any third-party payors, including private insurers or patients. Several states also require pharmaceutical companies to report expenses relating to the marketing and promotion of pharmaceutical products in those states and to report gifts and payments to individual health care providers in those states. Some of these states also prohibit certain marketing-related activities, including the provision of gifts, meals, or other items to certain health care providers, and restrict the ability of manufacturers to offer co-pay support to patients for certain prescription drugs. Some states require the posting of information relating to clinical studies and their outcomes. Some states and cities require identification or licensing of sales representatives. In addition, several states require pharmaceutical companies to implement compliance programs or marketing codes.

- Similar restrictions are imposed on the promotion and marketing of medicinal products in the EU Member States and other countries, including restrictions prohibiting the promotion of a compound prior to its approval. Laws (including those governing promotion, marketing and anti-kickback provisions), industry regulations and professional codes of conduct often are strictly enforced. Even in those countries where we may decide not to directly promote or market our products, inappropriate activity by our international distribution partners could have implications for us.

The shifting commercial compliance environment and the need to build and maintain robust and expandable systems to comply with different compliance or reporting requirements in multiple jurisdictions increase the possibility that we or our partners may fail to comply fully with one or more of these requirements. Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations may involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with applicable fraud and abuse or other healthcare laws and regulations or guidance. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, disgorgement, exclusion from government funded healthcare programs, such as Medicare and Medicaid in the US and similar programs outside the US, contractual damages, diminished profits and future earnings, and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our financial results. If any of the physicians or other providers or entities with whom we do or expect to do business are found to not be in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs. Even if we are not determined to have violated these laws, government investigations into these issues typically require the expenditure of significant resources and generate negative publicity, which could harm our financial condition and divert resources and the attention of our management from operating our business.

Our business and operations, including the use of hazardous and biological materials may result in liabilities with respect to environmental, health and safety matters.

Our research and development activities involve the controlled use of potentially hazardous substances, including chemical, biological and radioactive materials. In addition, our operations produce hazardous waste products, including hazardous waste. Federal, state and local laws and regulations govern the use, manufacture, management, storage, handling and disposal of hazardous materials and wastes. We may incur significant additional costs or liabilities to comply with, or for violations of, these and other applicable laws in the future. Also, even if we are in compliance with applicable laws, we cannot completely eliminate the risk of contamination or injury resulting from hazardous materials and we may incur liability as a result of any such contamination or injury. Further, in the event of a release of or exposure to hazardous materials, including at the sites we currently or formerly operate or at sites such as landfills where we send wastes for disposal, we could be held liable for cleanup costs or damages or subject to other costs or penalties and such liability could exceed our resources. We do not have any insurance for liabilities arising from hazardous materials or under environmental laws. Compliance with or liability under applicable environmental laws and regulations or with respect to hazardous materials may be expensive, and current or future environmental regulations may impair our research, development and production efforts, which could harm our business, which could cause the price of our securities to fall.

RISKS RELATING TO OUR ORDINARY SHARES

The market price for our shares has and may continue to fluctuate widely and may result in substantial losses for purchasers of our ordinary shares.

The market price for our shares has and may continue to fluctuate widely and may result in substantial losses for purchasers of our ordinary shares. To the extent that low trading volumes for our ordinary shares continues, our stock price may fluctuate significantly more than the stock market as a whole or the stock prices of similar companies. Without a larger public float of actively traded shares, our ordinary shares are likely to be more sensitive to changes in sales volumes, market fluctuations and events or perceived events with respect to our business, than the shares of common stock of companies with broader public ownership, and as a result, the trading prices for our ordinary shares may be more volatile. Among other things, trading of a relatively small volume of ordinary shares may have a greater effect on the trading price than would be the case if our public float of actively traded shares were larger. In addition, as further described below under the risk factor entitled "*—Concentration of ownership will limit your ability to influence corporate matters,*" a number of shareholders hold large concentrations of our shares which, if sold within a relatively short timeframe, could cause the price of our shares to drop significantly. In addition, as a result of the exchangeable note offering by GSK, up to 9,644,792 ordinary shares held by GSK could become freely tradeable after September 1, 2020, if holders of the GSK Notes were to exchange their notes for our ordinary shares, although our current stock price is below the exchange price.

Market prices for securities of biotechnology and biopharmaceutical companies have been highly volatile, and we expect such volatility to continue for the foreseeable future, so that investment in our ordinary shares involves substantial risk. Additionally, the stock market from time to time has experienced significant price and volume fluctuations unrelated to the operating performance of particular companies.

The following are some of the factors that may have a significant effect on the market price of our ordinary shares:

- any adverse developments or results or perceived adverse developments or results with respect to YUPELRI, including without limitation, lower than expected sales of YUPELRI, difficulties or delays encountered with regard to the FDA or other regulatory authorities in this program or any indication from clinical or non-clinical studies that YUPELRI is not safe or efficacious;

- any adverse developments or results or perceived adverse developments or results with respect to the GSK Partnered Respiratory Programs including, without limitation, lower than expected sales of TRELEGY, difficulties or delays encountered with regard to the FDA or other regulatory authorities in these programs or any indication from clinical or non-clinical studies that the compounds in such programs are not safe or efficacious;

- any adverse developments or results or perceived adverse developments or results with respect to our key clinical development programs, including, without limitation, any delays in development in these programs, any halting of development in these programs, any difficulties or delays encountered with regard to the FDA or other regulatory authorities in these programs (including any class-based risks that emerge as a FDA or other regulatory agency focus), or any indication from clinical or non-clinical studies that the compounds in such programs are not safe or efficacious;

- any announcements of developments with, or comments by, the FDA or other regulatory authorities with respect to products we or our partners have under development, are manufacturing or have commercialized;

- any adverse developments or disagreements or perceived adverse developments or disagreements with respect to our relationship with Innoviva, such as our 2019 and 2021 arbitration proceedings with them concerning their use of TRC funds, or the relationship of Innoviva or TRC on the one hand and GSK on the other hand, including any such developments or disagreements resulting from or relating to the TRC LLC Agreement or to the Spin-Off;

- any adverse developments or perceived adverse developments with respect to our relationship with any of our research, development or commercialization partners, including, without limitation, disagreements that may arise between us and any of those partners;
- any adverse developments or perceived adverse developments in our programs with respect to partnering efforts or otherwise;
- announcements of patent issuances or denials, technological innovations or new commercial products by us or our competitors;
- publicity regarding actual or potential study results or the outcome of regulatory review relating to products under development by us, our partners or our competitors;
- regulatory developments in the US and foreign countries;
- announcements with respect to governmental or private insurer reimbursement policies;
- announcements of equity or debt financings;
- possible impairment charges on non-marketable equity securities;
- economic and other external factors beyond our control, such as the COVID-19 pandemic and fluctuations in interest rates;
- loss of key personnel;
- likelihood of our ordinary shares to be more sensitive to changes in sales volume, market fluctuations and events or perceived events with respect to our business due to our small public float;
- low public market trading volumes for our ordinary shares related in part to the concentration of ownership of our shares;
- the sale of large concentrations of our shares, which may be more likely to occur due to the concentration of ownership of our shares, such as what we experienced when our largest shareholder, Woodford Investment Management Limited, divested its holdings in 2019 or which may occur as a result of the exchangeable note offering by GSK if holders of the GSK Notes were to exchange their notes for our ordinary shares;
- developments or disputes as to patent or other proprietary rights;
- approval or introduction of competing products and technologies;
- results of clinical trials;
- failures or unexpected delays in timelines for our potential products in development, including the obtaining of regulatory approvals;
- delays in manufacturing adversely affecting clinical or commercial operations;
- fluctuations in our operating results;
- market reaction to announcements by other biotechnology or pharmaceutical companies;

- initiation, termination or modification of agreements with our collaborators or disputes or disagreements with collaborators;
- litigation or the threat of litigation;
- public concern as to the safety of product candidates or medicines developed by us; and
- comments and expectations of results made by securities analysts or investors.

If any of these factors causes us to fail to meet the expectations of securities analysts or investors, or if adverse conditions prevail or are perceived to prevail with respect to our business, the price of the ordinary shares would likely drop significantly. For example, our stock price dropped significantly when we announced that izencitinib did not meet its primary endpoint in our Phase 2b/3 induction and maintenance study of izencitinib in ulcerative colitis. In addition, though none has been filed to our knowledge, a significant drop in the price of a company's securities often leads to the filing of securities class action litigation against the company. This type of litigation against us could result in substantial costs and a diversion of management's attention and resources.

Concentration of ownership will limit your ability to influence corporate matters.

Based on our review of publicly available filings, as of December 31, 2021, our three largest shareholders collectively owned 39.2% of our outstanding ordinary shares. These shareholders could control the outcome of actions taken by us that require shareholder approval, including a transaction in which shareholders might receive a premium over the prevailing market price for their shares.

Certain provisions in our constitutional and other documents may discourage our acquisition by a third-party, which could limit your opportunity to sell shares at a premium.

Our constitutional documents include provisions that could limit the ability of others to acquire control of us, modify our structure or cause us to engage in change-of-control transactions, including, among other things, provisions that:

- require supermajority shareholder voting to effect certain amendments to our amended and restated memorandum and articles of association;
- establish a classified board of directors;
- restrict our shareholders from calling meetings or acting by written consent in lieu of a meeting;
- limit the ability of our shareholders to propose actions at duly convened meetings; and
- authorize our board of directors, without action by our shareholders, to issue preferred shares and additional ordinary shares.

In addition, in May 2018, our shareholders approved a resolution authorizing our board of directors to adopt a shareholder rights plan in the future intended to deter any person from acquiring more than 19.9% of our outstanding ordinary shares without the approval of our board of directors.

These provisions could have the effect of depriving you of an opportunity to sell your ordinary shares at a premium over prevailing market prices by discouraging third parties from seeking to acquire control of us in a tender offer or similar transaction.

Our shareholders may face difficulties in protecting their interests because we are incorporated under Cayman Islands law.

Our corporate affairs are governed by our amended and restated memorandum and articles of association, by the Companies Law (2020 Revision) of the Cayman Islands and by the common law of the Cayman Islands. The rights

of our shareholders and the fiduciary responsibilities of our directors under the laws of the Cayman Islands are different from those under statutes or judicial precedent in existence in jurisdictions in the US. Therefore, you may have more difficulty in protecting your interests than would shareholders of a corporation incorporated in a jurisdiction in the US, due to the different nature of Cayman Islands law in this area.

Shareholders of Cayman Islands exempted companies such as our company have no general rights under Cayman Islands law to inspect corporate records and accounts or to obtain copies of lists of shareholders. Our directors have discretion under our amended and restated memorandum and articles of association to determine whether or not, and under what conditions, our corporate records may be inspected by our shareholders, but are not obliged to make them available to our shareholders. This may make it more difficult for you to obtain the information needed to establish any facts necessary for a shareholder motion or to solicit proxies from other shareholders in connection with a proxy contest.

Our Cayman Islands counsel, Maples and Calder, is not aware of any reported class action having been brought in a Cayman Islands court. Derivative actions have been brought in the Cayman Islands courts, and the Cayman Islands courts have confirmed the availability for such actions. In most cases, the Company will be the proper plaintiff in any claim based on a breach of duty owed to it, and a claim against (for example) our officers or directors usually may not be brought by a shareholder. However, based on English authorities, which would in all likelihood be of persuasive authority and be applied by a court in the Cayman Islands, exceptions to the foregoing principle apply in circumstances in which:

- a company is acting, or proposing to act, illegally or beyond the scope of its authority;
- the act complained of, although not beyond the scope of the authority, could be effected if duly authorized by more than the number of votes which have actually been obtained; or
- those who control the company are perpetrating a “fraud on the minority.”

A shareholder may have a direct right of action against the company where the individual rights of that shareholder have been infringed or are about to be infringed.

There is uncertainty as to shareholders’ ability to enforce certain foreign civil liabilities in the Cayman Islands.

We are incorporated as an exempted company limited by shares with limited liability under the laws of the Cayman Islands. A material portion of our assets are located outside of the US. As a result, it may be difficult for our shareholders to enforce judgments against us or judgments obtained in US courts predicated upon the civil liability provisions of the federal securities laws of the US or any state of the US.

We understand that the courts of the Cayman Islands are unlikely (i) to recognize or enforce against Theravance Biopharma judgments of courts of the US predicated upon the civil liability provisions of the securities laws of the US or any State; and (ii) in original actions brought in the Cayman Islands, to impose liabilities against Theravance Biopharma predicated upon the civil liability provisions of the securities laws of the US or any State, on the grounds that such provisions are penal in nature. However, in the case of laws that are not penal in nature, although there is no statutory enforcement in the Cayman Islands of judgments obtained in the US, the courts of the Cayman Islands will recognize and enforce a foreign money judgment of a foreign court of competent jurisdiction without retrial on the merits based on the principle that a judgment of a competent foreign court imposes upon the judgment debtor an obligation to pay the sum for which judgment has been given provided certain conditions are met. For a foreign judgment to be enforced in the Cayman Islands, such judgment must be final and conclusive and for a liquidated sum, and must not be in respect of taxes or a fine or penalty, inconsistent with a Cayman Islands’ judgment in respect of the same matter, impeachable on the grounds of fraud or obtained in a manner, and or be of a kind the enforcement of which is, contrary to natural justice or the public policy of the Cayman Islands (awards of punitive or multiple damages may well be held to be contrary to public policy). A Cayman Islands court, including the Grand Court of the Cayman Islands, may stay proceedings if concurrent proceedings are being brought elsewhere, which would delay proceedings and make it more difficult for our shareholders to bring action against us.

If securities or industry analysts cease coverage of us or do not publish research, or publish inaccurate or unfavorable research, about our business, the price of our ordinary shares and trading volume could decline.

The trading market for our ordinary shares depends in part on the research and reports that securities or industry analysts publish about us or our business. If few securities analysts commence coverage of us, or if industry analysts cease coverage of us, the trading price for our ordinary shares could be negatively affected. If one or more of the analysts who cover us downgrade our ordinary shares or publish inaccurate or unfavorable research about our business or if our results fail to meet the expectations of these analysts, the price of our ordinary shares would likely decline. If one or more of these analysts cease coverage of us or fail to publish reports on us regularly, demand for our ordinary shares could decrease, which might cause our share price and trading volume to decline.

We do not anticipate paying any cash dividends on our capital shares in the foreseeable future; as a result, capital appreciation, if any, of our ordinary shares will be your sole source of gain for the foreseeable future.

We have never declared or paid cash dividends on our capital shares. We do not anticipate paying any cash dividends on our capital shares in the foreseeable future. We currently intend to retain all available funds and any future earnings to fund the development and growth of our business. In addition, the terms of any future debt financing arrangement may contain terms prohibiting or limiting the amount of dividends that may be declared or paid on our ordinary shares. As a result, capital appreciation, if any, of our ordinary shares will be your sole source of gain for the foreseeable future.

ITEM 1B. UNRESOLVED STAFF COMMENTS

Not applicable.

ITEM 2. PROPERTIES

Our principal physical properties in the US consist of approximately 162,000 square feet of office and laboratory space leased in two buildings in South San Francisco, California. The South San Francisco lease expires in May 2030. Our Irish subsidiary operates from approximately 6,100 square feet of leased office space in Dublin, Ireland, and the lease expires in April 2027. As a result of our corporate restructuring announced in September 2021, we are evaluating options to reduce our leased space to meet our current and future needs.

ITEM 3. LEGAL PROCEEDINGS

Not applicable.

ITEM 4. MINE SAFETY DISCLOSURES

Not applicable.

PART II

ITEM 5. MARKET FOR THE REGISTRANT'S COMMON EQUITY, RELATED STOCKHOLDER MATTERS AND ISSUER PURCHASES OF EQUITY SECURITIES

Our ordinary shares have traded on The Nasdaq Global Market under the symbol "TBPH" since June 3, 2014. As of February 21, 2022, there were 54 shareholders of record of our ordinary shares. As many of our ordinary shares are held by brokers and other institutions on behalf of shareholders, we are unable to estimate the total number of underlying shareholders represented by these shareholders of record.

Dividend Policy

We currently intend to retain any future earnings to finance our research and development efforts. We have never declared or paid cash dividends on our ordinary shares and do not intend to declare or pay cash dividends on our ordinary shares in the foreseeable future.

Equity Compensation Plans

The following table provides certain information with respect to all of our equity compensation plans in effect as of December 31, 2021:

Plan Category	Number of Securities to be Issued Upon Exercise of Outstanding Options, Warrants and Rights (a)	Weighted-Average Exercise Price of Outstanding Options, Warrants and Rights	Number of Securities Remaining Available for Future Issuance Under Equity Compensation Plans (excluding securities reflected in column (a))
Options	2,670,158	$ 25.18	2,702,513
Restricted shares	8,353,849	n/a	n/a
Employee share purchase plan	n/a	n/a	2,658,006
Equity compensation plans approved by security holders	11,024,007	$ 25.18	5,360,519
Options	201,410	$ 17.17	218,611
Equity compensation plans not approved by security holders	201,410	$ 17.17	218,611
Total	11,225,417	$ 24.62	5,579,130

We have three equity compensation plans — our 2013 Equity Incentive Plan (the "2013 EIP"), our 2013 Employee Share Purchase Plan (the "2013 ESPP"), and our 2014 New Employee Equity Incentive Plan (the "2014 NEEIP"). At inception of the plans, we were authorized to issue 5,428,571 ordinary shares under the 2013 EIP and 857,142 ordinary shares under the 2013 ESPP, and 750,000 ordinary shares under the 2014 NEEIP.

The 2013 EIP provides for the issuance of share-based awards, including restricted shares, restricted share units, options, share appreciation rights ("SARs") and other equity-based awards, to our employees, officers, directors and consultants. As of January 1 of each year, commencing on January 1, 2015 and ending on (and including) January 1, 2023, the aggregate number of ordinary shares that may be issued under the 2013 EIP shall automatically increase by a number equal to the least of (i) 5% of the total number of ordinary shares outstanding on December 31 of the prior year; (ii) 3,428,571 ordinary shares; or (iii) a number of ordinary shares determined by our board of directors. Options may be granted with an exercise price not less than the fair market value of the ordinary shares on the grant date. Under the terms of our 2013 EIP, options granted to employees generally have a maximum term of 10 years and vest over a four-year period from the date of grant; 25% vest at the end of one year, and 75% vest monthly over the remaining three years. We may grant options with different vesting terms from time to time. Unless an employee's termination of service is due to disability or death, upon termination of service, any unexercised vested options will generally be forfeited at the end of three months or the expiration of the option, whichever is earlier.

Under the 2013 ESPP, our officers and employees may purchase ordinary shares through payroll deductions at a price equal to 85% of the lower of the fair market value of the ordinary share at the beginning of the offering period or at the end of each applicable purchase period. As of January 1 of each year, commencing on January 1, 2015 and ending on (and including) January 1, 2033, the aggregate number of ordinary shares that may be issued under the 2013 ESPP shall automatically increase by a number equal to the least of (i) 1% of the total number of ordinary shares outstanding on December 31 of the prior year; (ii) 857,142 ordinary shares; or (iii) a number of ordinary shares determined by our board of directors. The ESPP generally provides for consecutive and overlapping offering periods of 24 months in duration, with each offering period generally composed of four consecutive six-month purchase periods. The purchase periods end on either May 15 or November 15. ESPP contributions are limited to a maximum of 15% of an employee's eligible compensation. Our 2013 ESPP also includes a feature that provides for the existing offering period to terminate and for participants in that offering period to automatically be enrolled in a new offering period when the fair market value of an ordinary share at the beginning of a subsequent offering period falls below the fair market value of an ordinary share on the first day of such offering period.

The 2014 NEEIP provides for the issuance of share-based awards, including restricted shares, restricted share units, non-qualified options and SARs, to our employees. Options may be granted with an exercise price not less than the fair market value of the ordinary shares on the grant date. Under the terms of our 2014 NEEIP, options granted to employees generally have a maximum term of 10 years and vest over a four-year period from the date of grant; 25% vest at the end of one year, and 75% vest monthly over the remaining three years. We may grant options with different vesting terms from time to time. Unless an employee's termination of service is due to disability or death, upon termination of service, any unexercised vested options will generally be forfeited at the end of three months or the expiration of the option, whichever is earlier.

Additional information regarding share-based compensation is included in *"Item 8, Note 1. Organization and Summary of Significant Accounting Policies,"* and *"Item 8, Note 10. Share-Based Compensation,"* to the consolidated financial statements appearing in this Annual Report on Form 10-K.

Share Performance Graph

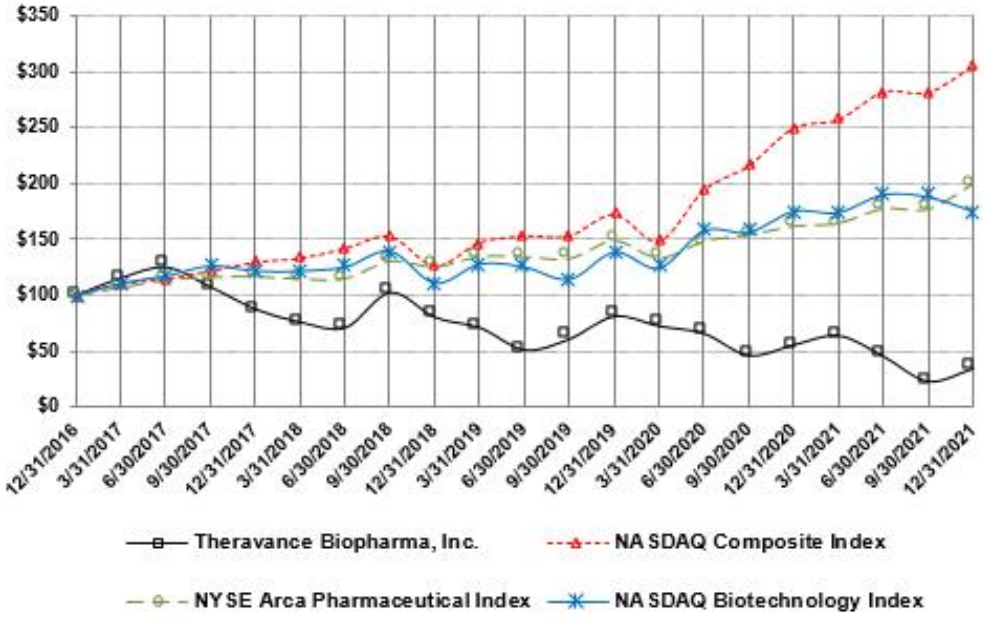
The graph set forth below compares the cumulative total shareholder return on our ordinary shares from December 31, 2016 through December 31, 2021, with the cumulative total return of (i) the Nasdaq Composite Index, (ii) the NYSE Arca Pharmaceutical Index (previously labeled as the Nasdaq Pharmaceutical Index) and (iii) the Nasdaq Biotechnology Index over the same period. This graph assumes the investment of $100 on December 31, 2016 in each of (1) our ordinary shares, (2) the Nasdaq Composite Index, (3) the NYSE Arca Pharmaceutical Index and (4) the Nasdaq Biotechnology Index, and assumes the reinvestment of dividends, if any, although dividends have never been declared on our ordinary shares.

The comparisons shown in the graph below are based upon historical data. We caution that the price performance shown in the graph below is not necessarily indicative of, nor is it intended to forecast, the potential future performance of our ordinary shares.

Notwithstanding anything to the contrary set forth in any of our previous or future filings under the Securities Act or the Exchange Act that might incorporate this Annual Report on Form 10-K or future filings made by us under those statutes, this Performance Graph section shall not be deemed filed with the SEC and shall not be deemed incorporated by reference into any of those prior filings or into any future filings made by us under those statutes.

COMPARISON OF CUMULATIVE TOTAL RETURN *

Among Theravance Biopharma, Inc., the NASDAQ Composite Index,
the NYSE Arca Pharmaceutical Index and the NASDAQ Biotechnology Index



* Represents the cumulative return on investment assuming an investment of $100 in our ordinary shares or the indices on December 31, 2016, including the reinvestment of dividends.

$100 Investment in TBPH Shares or Index	TBPH	NASDAQ Composite Index	NYSE Arca Pharmaceutical Index	NASDAQ Biotechnology Index
December 31, 2016	$ 100.00	$ 100.00	$ 100.00	$ 100.00
December 31, 2017	87.48	129.73	116.58	121.63
December 31, 2018	80.27	126.08	125.31	110.85
December 31, 2019	81.21	172.41	148.35	138.69
December 31, 2020	55.74	250.08	161.32	175.33
December 31, 2021	34.66	305.63	199.02	175.37

ITEM 6. [RESERVED]

ITEM 7. MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

Our Management's Discussion and Analysis ("MD&A") is intended to facilitate an understanding of our results of operations, as well as our liquidity and capital resources. Additionally, it describes accounting policies and estimates that management has deemed as "critical accounting policies and estimates." This MD&A should be read in conjunction with our consolidated financial statements and notes included in this Annual Report on Form 10-K. The information contained in this MD&A or set forth elsewhere in this Annual Report on Form 10-K, including information with respect to our plans and strategy for our business, our operating expenses, and future payments under our collaboration agreements, includes forward-looking statements within the meaning of Section 27A of the Securities Act of 1933 (the "Securities Act"), and Section 21E of the Securities Exchange Act of 1934 (the "Exchange Act"). Such statements are based upon current expectations that involve risks and uncertainties. You should review the section entitled *"Risk Factors"* in Item 1A of Part I above for a discussion of important factors that could cause actual results to differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis. See the section entitled *"Special Note regarding Forward-Looking Statements"* on page 3 for more information.

Management Overview

Theravance Biopharma is a biopharmaceutical company primarily focused on the discovery, development and commercialization of respiratory medicines. Our core purpose is to *create medicines that make a difference*® in people's lives.

In pursuit of our purpose, we leverage decades of respiratory expertise to discover and develop transformational medicines that make a difference. These efforts have led to the development of the US FDA approved YUPELRI® (revefenacin) inhalation solution indicated for the maintenance treatment of patients with COPD. Our respiratory pipeline of internally discovered programs is targeted to address significant patient respiratory needs.

We have an economic interest in potential future payments from GSK pursuant to our agreements with Innoviva" relating to certain programs, including TRELEGY.

Strategic Actions to Focus on Respiratory Diseases

Given clinical results from our late-stage development programs, in September 2021, our board of directors approved a plan to focus our resources on our most promising respiratory programs and reduce the size of the Company in order to maximize shareholder value. At completion, the corporate restructuring (the "Restructuring") will result in us reducing headcount by approximately 75%, an estimated 270 positions, through a reduction in our workforce. Approximately 75% of the total reduction in workforce occurred at the end November 2021, and the remainder will be completed at the end of February 2022.

As a result of the Restructuring, we expect to realize estimated operating expense savings (excluding share-based compensation and any one-time restructuring, severance, and termination costs) of approximately $170.0 million. We estimate that we will incur total Restructuring and related expenses of approximately $32.0 million comprised of $17.0 million in cash expenses and $15.0 million in non-cash expenses. These expenses are primarily comprised of severance and other related costs. In 2021, we recognized $20.1 million of the Restructuring expenses comprised of $11.5 million in cash-related expenses and $8.6 million in non-cash expenses.

We expect to recognize the majority of the remaining approximate $12.0 million in Restructuring expenses, comprised of $5.0 million in cash-related expenses and $7.0 million in non-cash expenses, in the first quarter of 2022 and the balance by the third quarter of 2022. The remaining Restructuring expense estimates are subject to a number of assumptions, and actual final amounts may differ. We may also incur additional costs not currently contemplated due to events that may occur as a result of, or that are associated with, the Restructuring.

The go-forward organization leverages our expertise in developing and commercializing respiratory therapeutics. We intend to significantly narrow our R&D focus on our core respiratory assets, including a clinical study

with Viatris Inc. (“Viatris”) intended to provide data to support a possible label update for YUPELRI, which would capture more of YUPELRI’s addressable market and further strengthen its competitive advantage, and investment in our inhaled Janus kinase inhibitor portfolio, with focus on our most advanced clinical candidate, nezulcitinib, initially targeting acute lung injury. We will also continue to explore strategic partnerships for both core and non-core assets to unlock value. All of these actions drive towards our goal to maximize shareholder value.

After implementing these strategic actions, we plan to become sustainably cash flow positive beginning in the second half of 2022, and we will work to optimize our capital structure in order to maximize total shareholder returns.

Critical Accounting Policies and Estimates

Our discussion and analysis of our financial condition and results of operations is based on our consolidated financial statements, which have been prepared in accordance with US Generally Accepted Accounting Principles (“GAAP”). The preparation of these financial statements requires us to make estimates and assumptions that affect the reported amounts of revenues, expenses, assets, liabilities, and other related disclosures. Our estimates are based on our historical experience and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. The extent to which the COVID-19 pandemic will continue to directly or indirectly impact our business, results of operations and financial condition, including these estimates, will depend on future developments that are highly uncertain and may be impacted by the emergence of new information concerning the COVID-19 pandemic, ongoing spread of the disease across the US and the globe, and the actions taken to contain or treat the disease, including vaccine availability, distribution, acceptance and effectiveness. Actual results may differ from these estimates under different assumptions or conditions. We believe that the accounting policies and estimates discussed below are essential to understanding our operating results and financial condition, as these policies and estimates relate to the more significant areas involving management’s judgments.

Revenue Recognition

We recognize revenue under Accounting Standards Codification (“ASC”), Topic 606, *Revenue from Contracts with Customers* (“ASC 606”). Under ASC 606, an entity recognizes revenue when its customer obtains control of promised goods or services, in an amount that reflects the consideration which the entity expects to receive in exchange for those goods or services. To determine revenue recognition for arrangements that an entity determines are within the scope of ASC 606, an entity performs the following five steps: (i) identify the contract(s) with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when (or as) the entity satisfies a performance obligation.

At contract inception, once the contract is determined to be within the scope of ASC 606, we identify the performance obligations in the contract by assessing whether the goods or services promised within each contract are distinct. We then recognize revenue for the amount of the transaction price that is allocated to the respective performance obligation when (or as) the performance obligation is satisfied.

Collaborative Arrangements under ASC 606

We enter into collaborative arrangements with partners that fall under the scope of Accounting Standards Codification, Topic 808, *Collaborative Arrangements* (“ASC 808”). While these arrangements are in the scope of ASC 808, we may analogize to ASC 606 for some aspects of these arrangements. We analogize to ASC 606 for certain activities within collaborative arrangements for the delivery of a good or service (i.e., a unit of account) that is part of our ongoing major or central operations. Revenue recognized by analogizing to ASC 606 is recorded as “collaboration revenue” or “licensing revenue” whereas, revenue recognized in accordance with ASC 808 is recorded on a separate collaboration revenue line on the consolidated statements of operations.

The terms of our collaborative arrangements typically include one or more of the following: (i) up-front fees; (ii) milestone payments related to the achievement of development, regulatory, or commercial goals; (iii) royalties on net sales of licensed products; (iv) reimbursements or cost-sharing of research and development expenses; and (v) profit/loss sharing arising from co-promotion arrangements. Each of these payments results in collaboration revenues or an offset

against research and development expense. Where a portion of non-refundable up-front fees or other payments received is allocated to continuing performance obligations under the terms of a collaborative arrangement, they are recorded as deferred revenue and recognized as collaboration revenue when (or as) the underlying performance obligation is satisfied.

As part of the accounting for these arrangements, we must develop estimates and assumptions that require judgment to determine the underlying stand-alone selling price for each performance obligation which determines how the transaction price is allocated among the performance obligations. The estimation of the stand-alone selling price may include such estimates as, forecasted revenues or costs, development timelines, discount rates and probabilities of technical and regulatory success. We evaluate each performance obligation to determine if they can be satisfied at a point in time or over time, and we measure the services delivered to our collaborative partner which are periodically reviewed based on the progress of the related program. The effect of any change made to an estimated input component and, therefore revenue or expense recognized, would be recorded as a change in estimate. In addition, variable consideration (e.g., milestone payments) must be evaluated to determine if it is constrained and, therefore, excluded from the transaction price.

Up-front Fees: If a license to our intellectual property is determined to be distinct from the other performance obligations identified in the arrangement, we recognize collaboration revenues from the transaction price allocated to the license when the license is transferred to the licensee and the licensee is able to use and benefit from the license. For licenses that are bundled with other promises, we utilize judgment to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time and, if over time, the appropriate method of measuring progress for purposes of recognizing collaboration revenue from the allocated transaction price. For example, when we receive up-front fees for the performance of research and development services, or when research and development services are not considered to be distinct from a license, we recognize collaboration revenue for those units of account over time using a measure of progress. We evaluate the measure of progress each reporting period and, if necessary, adjust the measure of performance and related revenue or expense recognition as a change in estimate.

Milestone Payments: At the inception of each arrangement that includes milestone payments (variable consideration), we evaluate whether the milestones are considered probable of being reached and estimate the amount to be included in the transaction price using the most likely amount method. If it is probable that a significant revenue reversal would not occur, the associated milestone value is included in the transaction price. Milestone payments that are not within our or the collaborative partner's control, such as non-operational developmental and regulatory approvals, are generally not considered probable of being achieved until those approvals are received. At the end of each reporting period, we re-evaluate the probability of achievement of milestones that are within our or the collaborative partner's control, such as operational developmental milestones and any related constraint, and if necessary, adjust our estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis, which would affect collaboration revenues and earnings in the period of adjustment. Revisions to our estimate of the transaction price may also result in negative collaboration revenues and earnings in the period of adjustment.

Royalties: For arrangements that include sales-based royalties, including commercial milestone payments based on the level of sales, and the license is deemed to be the predominant item to which the royalties relate, we recognize revenue at the later of (i) when the related sales occur, or (ii) when the performance obligation to which some or all of the royalty has been allocated has been satisfied (or partially satisfied). Our income earned related to TRELEGY sales is included within "income from our investment in TRC, LLC" on the consolidated statements of operations.

Reimbursement, cost-sharing and profit-sharing payments: Under certain collaborative arrangements, we have been reimbursed for a portion of our research and development expenses or participate in the cost-sharing of such research and development expenses. Such reimbursements and cost-sharing arrangements have been reflected as a reduction of research and development expense in our consolidated statements of operations, as we do not consider performing research and development services for reimbursement to be a part of our ongoing major or central operations.

Research and Development Expenses

We incur substantial expenses associated with our clinical trials. Accounting for clinical trials relating to activities performed by clinical research organizations ("CROs"), contract manufacturing organizations ("CMOs") and other external vendors requires management to exercise significant estimates in regard to the timing and accounting for these expenses. We estimate costs of research and development activities conducted by service providers, which include, the conduct of sponsored research, preclinical studies, and contract manufacturing activities. The diverse nature of services being provided under CRO and other arrangements, the different compensation arrangements that exist for each type of service and the lack of timely information related to certain clinical activities complicates the estimation of accruals for services rendered by CROs, CMOs and other vendors in connection with clinical trials.

Research and development ("R&D") expenses are recorded in the period that services are rendered or goods are received. R&D expenses consist of salaries and benefits, laboratory supplies and facility costs, as well as fees paid to third parties that conduct certain R&D activities on our behalf, net of certain external R&D expenses reimbursed under our collaborative arrangements.

As part of the process of preparing our consolidated financial statements, we are required to estimate and accrue certain R&D expenses. This process involves the following:

- identifying services that have been performed on our behalf and estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of actual cost;
- estimating and accruing expenses in our consolidated financial statements as of each balance sheet date based on facts and circumstances known to us at the time; and
- periodically confirming the accuracy of our estimates with selected service providers and making adjustments, if necessary.

Examples of estimated R&D expenses that we accrue include:

- fees paid to CROs in connection with preclinical and toxicology studies and clinical studies;
- fees paid to investigative sites in connection with clinical studies;
- fees paid to CMOs in connection with the production of product and clinical study materials; and
- professional service fees for consulting and related services.

We base our expense accruals related to clinical studies on our estimates of the services received and efforts expended pursuant to contracts with multiple research institutions and CROs that conduct and manage clinical studies on our behalf. The financial terms of these agreements vary from contract to contract and may result in uneven payment flows. Payments under some of these contracts depend on factors, such as the successful enrollment of patients and the completion of clinical study milestones. Our service providers typically invoice us monthly in arrears for services performed. In accruing service fees, we estimate the time period over which services will be performed and the level of effort to be expended in each period. If we do not identify costs that we have begun to incur or if we underestimate or overestimate the level of services performed or the costs of these services, our actual expenses could differ from our estimates.

To date, we have not experienced significant changes in our estimates of accrued R&D expenses after a reporting period. However, due to the nature of estimates, there is no assurance that we will not make changes to our estimates in the future as we become aware of additional information about the status or conduct of our clinical studies and other R&D activities. Such changes in estimates will be recognized as R&D expenses in the period that the change in estimate occurs.

Theravance Respiratory Company, LLC ("TRC")

Through our 85% equity interest in TRC, we are entitled to receive an 85% economic interest in any future payments made by GSK under the strategic alliance agreement and under the portion of the collaboration agreement assigned to TRC (net of TRC expenses paid and the amount of cash, if any, expected to be used by TRC pursuant to the TRC LLC Agreement over the next four fiscal quarters). The primary drug program assigned to TRC is TRELEGY.

We analyzed our ownership, contractual and other interests in TRC to determine if TRC is a variable-interest entity ("VIE"), whether we have a variable interest in TRC and the nature and extent of that interest. We determined that TRC is a VIE. The party with the controlling financial interest, the primary beneficiary, is required to consolidate the entity determined to be a VIE. Therefore, we also assessed whether we are the primary beneficiary of TRC based on the power to direct its activities that most significantly impact its economic performance and our obligation to absorb its losses or the right to receive benefits from it that could potentially be significant to TRC. Based on our assessment, we determined that we are not the primary beneficiary of TRC, and, as a result, we do not consolidate TRC in our consolidated financial statements. TRC is recognized in our consolidated financial statements under the equity method of accounting.

Income related to our equity ownership of TRC is reflected within our consolidated statements of operations and is classified as non-operating income. Amounts due from TRC that we believe to be collectable within one year and our equity in the net assets of TRC are reflected on our consolidated balance sheets as a current asset and a non-current asset, respectively. The portion of the Non-Recourse 2035 Notes classified as a current liability, if any, is based on the amount of royalties received, or receivable, as of December 31, 2021, that are expected to be collected from TRC and used to make a principal repayment on the Non-Recourse 2035 Notes within the next twelve months. The determination of the amounts likely to be received from TRC within the next twelve months requires significant judgement due to the significant variability of the amounts paid to the Company, as compared to the royalties due. Consequently, the actual amount paid to the holders of the 2035 Notes within twelve months of the reporting date may differ significantly from that recorded in the consolidated balance sheets.

Income Taxes

We utilize the asset and liability method of accounting for income taxes. Under this method, deferred tax assets and liabilities are determined based on differences between financial reporting and tax basis of assets and liabilities and are measured using enacted tax rates and laws that are anticipated to be in effect when the differences are expected to reverse. A valuation allowance is provided when it is more likely than not that some portion or all of a deferred tax asset will not be realized.

Our total unrecognized tax benefits of $75.0 million and $63.4 million, as of December 31, 2021 and December 31, 2020, respectively, may reduce the effective tax rate in the period of recognition. We currently have a full valuation allowance against our deferred tax assets, which would impact the timing of the effective tax rate benefit should any of our uncertain positions be favorably settled in the future.

We assess all material positions, including all significant uncertain positions, in all tax years that are still subject to assessment or challenge by relevant taxing authorities. Assessing an uncertain tax position begins with the initial determination of the position's sustainability and is measured at the largest amount of benefit that is greater than 50% likely to be realized upon ultimate settlement. As of each balance sheet date, unresolved uncertain tax positions must be reassessed, and we will determine whether the factors underlying the sustainability assertion have changed and whether the amount of the recognized tax benefit is still appropriate.

The recognition and measurement of tax benefits requires significant judgment. We have taken certain positions where we believe that our position is greater than 50% likely to be realized upon ultimate settlement and for which no reserve for uncertain tax positions has been recorded. If we do not ultimately realize the expected benefit of these positions, we will record additional income tax expenses in future periods. Judgments concerning the recognition and measurement of a tax benefit might change as new information becomes available.

Any tax levied or credited by a governmental taxing authority that is not based on our income is outside the scope of accounting for income taxes. Therefore, we record such items as a component in our loss before income taxes.

Results of Operations

The following tables set forth our results of operations for the periods presented. Management's commentary for the 2021 results compared to 2020 results are presented in the paragraphs below, and management's commentary for the 2020 results compared to the 2019 results are included in our Annual Report on Form 10-K for the year ended December 31, 2020, filed with the SEC on February 26, 2021.

Revenue

Revenue, as compared to the prior years, was as follows:

	Year Ended December 31,			Change			
				2021		2020	
(In thousands)	2021	2020	2019	$	%	$	%
Collaboration revenue	$ 11,463	$ 26,464	$ 31,250	$ (15,001)	(57)%	$ (4,786)	(15)%
Licensing revenue	—	1,500	28,500	(1,500)	NM	(27,000)	(95)
Viatris collaboration agreement	43,848	43,893	13,664	(45)	(0)	30,229	221
Total revenue	$ 55,311	$ 71,857	$ 73,414	$ (16,546)	(23)%	$ (1,557)	(2)%

NM: Not Meaningful

Collaboration revenue was $11.5 million in 2021, which represented a $15.0 million decrease from 2020. Collaboration revenue was primarily comprised of revenue recognized related to the $100.0 million upfront payment received in 2018 pursuant to the Janssen collaboration agreement that was entered into in February 2018. Janssen collaboration revenue is recognized for the R&D services we performed during the period based on a measure of our efforts toward satisfying the performance obligation relative to the total expected efforts or inputs to satisfy the performance obligation (e.g., costs incurred compared to total budgeted costs). The $15.0 million decrease in collaboration revenue compared to 2020 reflects the reduction of costs incurred to satisfy the remaining performance obligation related to the recently completed izencitinib Phase 2 study in ulcerative colitis and the closeout of the izencitinib Phase 2 study in Crohn's disease. As of December 31, 2021, we have recognized all of the revenue associated with the Janssen $100.0 million upfront payment.

Licensing revenue was $1.5 million in 2020 and was attributable to the achievement of a milestone related to the acceptance of a clinical trial application associated with our agreement with Viatris to develop and commercialize nebulized revefenacin in China and adjacent territories. We did not recognize any licensing revenue in 2021.

We are entitled to a share of US profits and losses (65% to Viatris; 35% to Theravance Biopharma) received in connection with commercialization of YUPELRI. In accordance with the applicable accounting guidance, amounts receivable from Viatris in connection with the commercialization of YUPELRI are recorded within the consolidated statements of operations as revenue from "Viatris collaboration agreement" irrespective of whether the overall collaboration is profitable. Amounts payable to Viatris in connection with the commercialization of YUPELRI, if any, are recorded within the consolidated statements of operations as a collaboration loss within selling, general and administrative expenses. Any reimbursement from Viatris attributed to the 65% cost-sharing of our R&D expenses is characterized as a reduction of R&D expense, as we do not consider performing R&D services for reimbursement to be a part of our ordinary operations.

In 2021 and 2020, we recognized $43.8 million and $43.9 million, respectively, in revenue from the Viatris collaboration agreement, which represented the receivables due from Viatris related to YUPELRI. While Viatris records the total net sales of YUPELRI within its own financial statements, Viatris collaboration agreement revenue in our financial statements includes our implied 35% share of net sales of YUPELRI for 2021 and 2020 of $56.7 million and $50.0 million, respectively. While institutions in some parts of the country are allowing more in-person access, in-person engagements remain below pre-pandemic levels. Total 2021 prescription volumes continue to grow across most specialties with volumes heading toward parity with 2020. However, prescription volumes in pulmonology remain

below pre-pandemic levels. Despite the challenges of the respiratory pandemic, dose demand for YUPELRI increased 25% in 2021 compared to 2020.

Research and Development

Our R&D expenses consist primarily of employee-related costs, external costs, and various allocable expenses. We budget total R&D expenses on an internal department level basis, and we manage and report our R&D activities across the following four cost categories:

1) Employee-related costs, which include salaries, wages and benefits;

2) Share-based compensation, which includes expenses associated with our equity plans;

3) External-related costs, which include clinical trial related expenses, other contract research fees, consulting fees, and contract manufacturing fees; and

4) Facilities and other, which include laboratory and office supplies, depreciation and other allocated expenses, which include general and administrative support functions, insurance and general supplies.

The following table summarizes our R&D expenses incurred, net of any reimbursements from collaboration partners, as compared to the prior years:

	Year Ended December 31,			Change 2021		Change 2020	
(In thousands)	2021	2020	2019	$	%	$	%
Employee-related	$ 48,612	$ 60,557	$ 64,531	$ (11,945)	(20)%	$ (3,974)	(6)%
Share-based compensation	25,634	31,294	28,953	(5,660)	(18)	2,341	8
External-related	90,194	135,114	92,921	(44,920)	(33)	42,193	45
Facilities, depreciation and other allocated expenses	29,217	33,988	32,843	(4,771)	(14)	1,145	3
Total research & development	$ 193,657	$ 260,953	$ 219,248	$ (67,296)	(26)%	$ 41,705	19 %

R&D expenses decreased by $67.3 million in 2021 compared to 2020, and the decrease was across all R&D categories. External-related expenses decreased by $44.9 million and was the largest contributor to the total R&D expense decrease. The decrease in external-related expenses was primarily due to the completion, or-near completion, of our late-stage clinical programs, primarily izencitinib and ampreloxetine. The decreases across the remaining R&D categories were primarily due to the Restructuring announced in September 2021 which resulted in significant reductions in employee-related expenses, share-based compensation expenses, and other allocated expenses of $11.9 million, $5.7 million, and $4.8 million, respectively. The reduction in employee-related expenses was primarily due to the reversal of the annual corporate bonus, and the reduction in share-based compensation was primarily due to a reduction in employee headcount. The reduction in other allocated expenses was primarily due to the decrease in allocated overhead costs from selling, general, and administrative expenses due to the Restructuring. Expenses that were directly attributed to the Restructuring are included in the *Restructuring and Related Expenses* section below.

Under certain of our collaborative arrangements, we receive partial reimbursement of employee-related costs and external costs, which have been reflected as a reduction of R&D expenses of $7.9 million, $10.1 million and $5.6 million for 2021, 2020, and 2019, respectively.

As a result of the Restructuring and our focus on our respiratory programs, we expect R&D expenses to continue to decrease over the next 12 months.

Selling, General and Administrative

Selling, general and administrative expenses, as compared to the prior years, were as follows:

(In thousands)	Year Ended December 31, 2021	2020	2019	Change 2021 $	2021 %	2020 $	2020 %
Selling, general and administrative	$ 99,296	$ 108,661	$ 106,081	$ (9,365)	(9)%	$ 2,580	2 %

Selling, general and administrative expenses decreased by $9.4 million in 2021 compared to 2020. The $9.4 million decrease was primarily attributed to the Restructuring and resulted in reductions in employee-related expenses, share-based compensation expenses, and external-related services. The decrease in employee-related expenses was primarily due to the reversal of the annual corporate bonus, and the reduction in share-based compensation was primarily due to a reduction in employee headcount. The decrease in external-related expenses was primarily due to a reduction in expenses related to the Restructuring. Expenses that were directly attributed to the Restructuring are included in the *Restructuring and Related Expenses* section below.

Share-based compensation expense related to selling, general and administrative expenses was $28.1 million, $31.7 million, and $31.5 million, in 2021, 2020, and 2019, respectively.

Through June 2021, we leased approximately 170,000 square feet of office and laboratory space in two buildings in South San Francisco, California, under a non-cancelable operating lease that ends in May 2030. In July 2021, we terminated approximately 8,000 square feet of office space in one of the buildings and returned the space to the building's landlord for their use. We determined that the termination would be accounted for as a lease modification under the applicable accounting guidance. As a result of the modification, we adjusted the value of our operating lease assets and liabilities in our consolidated balance sheets that resulted in a gain of $1.9 million in 2021. The $1.9 million gain was offset against facility expenses within selling, general and administrative expenses and then partially allocated to R&D expenses above.

Effective October 2021, we also subleased approximately 21,000 square feet of our South San Francisco office and laboratory space. Under the terms of the sublease agreement, the Company will receive an initial monthly base rent of $0.1 million, with annual base rent increases of 3%, and the subtenant's proportionate share of the building's operating expenses. In October 2021, we began recognizing the sublease income on a straight-line basis over the term of the sublease which ends in September 2028. The sublease income was be reflected as a reduction facility expenses within selling, general and administrative expenses and then partially allocated to R&D expenses above.

As a result of the Restructuring, we expect our selling, general and administrative expenses to significantly decrease over the next 12 months.

Restructuring and Related Expenses

Restructuring and related expenses, as compared to the prior years, were as follows:

(In thousands)	Year Ended December 31, 2021	2020	2019	Change 2021 $	2021 %	2020 $	2020 %
Restructuring and related expenses	$ 11,780	$ —	$ —	$ 11,780	NM %	$—	NM %
Share-based compensation expense (Non-cash)	8,362	—	—	8,362	NM	—	NM
Total restructuring and related expenses	$ 20,142	$ —	$ —	$ 20,142	NM %	$—	NM %

NM: Not Meaningful

Of the total $20.1 million in Restructuring and related expenses recognized in 2021, $10.5 million was related to R&D expenses and $9.6 million was related to selling, general and administrative expenses. The Restructuring and related expenses were primarily comprised of one-time severance payments, employee-related separation costs, retention costs, and other Restructuring-related expenses. The $20.1 million also included non-cash charges of $8.6 million

primarily related to the modification of equity awards for employees affected by the Restructuring and certain related awards for other employees.

We estimate that we will incur total Restructuring and related expenses of approximately $32.0 million comprised of $17.0 million in cash expenses associated with employee termination benefits and related costs and $15.0 million in non-cash expenses relating to the acceleration of equity-awards for employees affected by the Restructuring. We expect to recognize the majority of the remaining approximate $12.0 million in Restructuring and related expenses, comprised of $5.0 million in cash-related expenses and $7.0 million in non-cash expenses, in the first quarter of 2022 and the balance by the third quarter of 2022. The remaining Restructuring expense estimates are subject to a number of assumptions, and actual final amounts may differ. We may also incur additional costs not currently contemplated due to events that may occur as a result of, or that are associated with, the Restructuring.

We are also evaluated the impact of the Restructuring on the carrying value of our long-lived assets, such as property and equipment and operating lease assets. This process included evaluating the estimated remaining lives, significant changes in the use, and potential impairment charges related to our long-lived assets. Based on our evaluation, we determined that our long-lived assets were not impaired as of December 31, 2021, and we did not recognize any impairment charges related to the long-lived assets in 2021. However, we may incur additional costs not currently contemplated due to events that may occur because of, or that are associated with, the Restructuring.

Income from Investment in TRC, LLC

Income from investment in TRC, as compared to the prior years, was as follows:

				Change			
	Year Ended December 31,			2021		2020	
(In thousands)	2021	2020	2019	$	%	$	%
Income from investment in TRC, LLC	$ 103,987	$ 68,438	$ 33,705	$ 35,549	52 %	$ 34,733	103 %

The income from investment in TRC, LLC represented our share of the royalty payments from GSK to TRC on the net sales of TRELEGY (net of our share of TRC expenses paid and the amount of cash, if any, expected to be used by TRC pursuant to the TRC LLC Agreement over the next four fiscal quarters).

Income from investment in TRC, LLC increased by $35.5 million in 2021 compared to 2020 which included $8.5 million representing our share of the one-time fee that GSK paid to TRC upon termination of the MABA program in June 2020. The $104.0 million and $68.4 million in TRC income for 2021 and 2020, respectively, were recorded net of our share of TRC expenses of $3.4 million and $2.2 million, respectively. Our share of TRC expenses for both years were primarily comprised of TRC's legal and related expenses associated with the arbitration between Innoviva and TRC and us.

In connection with the issuance of our $380.0 million net principal amount Non-Recourse 2035 Notes in February 2020, 75% of the income from our investment in TRC is available only for payment of the Non-Recourse 2035 Notes and is not available to pay other creditor obligations or claims.

See *"Risk Factors—We do not control the commercialization of TRELEGY and we do not control TRC; accordingly the amount of royalties we receive will depend on, among other factors, GSK's ability to further commercialize TRELEGY and TRC's decisions concerning use of cash in accordance with the TRC LLC Agreement"* for additional information regarding our economic interest in TRC, LLC.

Interest Expense

Interest expense primarily consisted of interest payments due on the Convertible Senior 2023 Notes, the redeemed Non-Recourse 2033 Notes, and the Non-Recourse 2035 Notes, as well as, the amortization of the associated debt issuance costs. Interest expense, as compared to the prior year, was as follows:

				Change			
	Year Ended December 31,			2021		2020	
(In thousands)	2021	2020	2019	$	%	$	%
9.5% Non-recourse notes due 2035	$ (38,342)	$ (32,193)	$ —	$ (6,149)	19 %	$ (32,193)	NM %
9.0% Non-recourse notes due 2033	—	(3,845)	(23,315)	3,845	NM	19,470	(84)
3.25% Convertible senior notes due 2023	(8,547)	(8,547)	(8,547)	—	—	—	—
Total interest expense	$ (46,889)	$ (44,585)	$ (31,862)	$ (2,304)	5 %	$ (12,723)	40 %

NM: Not Meaningful

Interest expense increased by $2.3 million in 2021 compared to 2020 The $2.3 million increase was primarily attributed to additional interest expense incurred in 2021 related to an increase in principal balance of the Non-Recourse 2035 Notes. The increase in principal balance resulted from the February 2020 re-financing of the Non-Recourse 2033 Notes and interest payment shortfalls added to the principal balance as of the applicable interest payment dates.

Loss on Extinguishment of Debt

Loss on extinguishment of debt as compared to the comparable periods in the prior year, was as follows:

				Change			
	Year Ended December 31,			2021		2020	
(In thousands)	2021	2020	2019	$	%	$	%
Loss on extinguishment of debt	$ —	$ (15,464)	$ —	$ 15,464	NM %	$ (15,464)	NM %

NM: Not Meaningful

In 2020, we recognized a $15.5 million loss on the extinguishment of debt related to the issuance of the Non-Recourse 2035 Notes in February 2020. A portion of the proceeds from the Non-Recourse 2035 Notes were used to repay the outstanding balance of the Non-Recourse 2033 Notes that were issued in November 2018. The $15.5 million loss was comprised of a redemption premium related to the early repayment of the Non-Recourse 2033 Notes and the write-off of the previously deferred debt issuance costs related to the portion of the Non-Recourse 2033 Notes that was considered extinguished.

Interest and Other Income (Expense), net

Interest and other income (expense), net, as compared to the prior years, was as follows:

				Change			
	Year Ended December 31,			2021		2020	
(In thousands)	2021	2020	2019	$	%	$	%
Interest and other income (expense), net	$ 1,109	$ 4,441	$ 8,395	$ (3,332)	(75)%	$ (3,954)	(47)%
Costs related to GSK offering	—	(1,610)	—	1,610	NM	(1,610)	NM
Total interest and other income (expense), net	$ 1,109	$ 2,831	$ 8,395	$ (1,722)	(61)%	$ (5,564)	(66)%

NM: Not Meaningful

Interest and other income (expense), net, decreased by $1.7 million in 2021 compared to 2020. The decrease was primarily due to higher investment balances in 2020 following the issuance of the Non-Recourse 2035 Notes in February 2020, lower investment yields in 2021, and an increase in foreign currency losses in 2021.

In June 2020, GSK completed its previously announced offering of $300.0 million of exchangeable senior notes due 2023, $280.3 million of which are exchangeable into our ordinary shares that are held by GSK and its affiliates for investment purposes. The $1.6 million in costs were primarily comprised of financial advisory and legal-related costs incurred by us in connection with the GSK offering.

Provision for Income Tax Benefit

The provision for income tax benefit, as compared to the prior years, was as follows:

	Year Ended December 31,			Change			
				2021		2020	
(In thousands)	2021	2020	2019	$	%	$	%
Provision for income tax benefit	$ 151	$ 8,520	$ 5,222	$ (8,369)	(98)%	$ 3,298	63 %

The benefits for income tax were primarily due to the reversals of previously accrued contingent liabilities for uncertain tax positions due to a lapse of the statute of limitations. The $8.4 million decrease in income tax benefit in 2021 compared to 2020 was primarily due to a lower estimate of the uncertain tax positions taken with respect to transfer pricing and tax credits in comparison to 2020. Our provision for income tax expense differs from the expected statutory rate due to the valuation allowance on deferred tax assets.

We are currently under Internal Revenue Service (“IRS”) examination for the tax year ended December 31, 2018. We believe that an adequate provision has been made for any adjustments that may result from the tax examination.

Liquidity and Capital Resources

As of December 31, 2021, we had approximately $173.5 million in cash, cash equivalents, and investments in marketable securities (excluding restricted cash). To date, we have financed our operations primarily through public offerings of equity securities, private placements of equity and debt, revenue from collaboration and licensing arrangements and, to a lesser extent, revenue from product sales. As of December 31, 2021, we had outstanding (i) $230.0 million in principal Convertible Senior 2023 Notes and (ii) $392.6 million in principal Non-Recourse 2035 Notes which are stated net of a 5.0% retention by us in compliance with Regulation RR — Credit Risk Retention (17 C.F.R. Part 246).

The Non-Recourse 2035 Notes were issued on February 28, 2020 and are secured by all of the Triple Royalty Sub II LLC’s (the “Issuer II”) rights, title and interest as a holder of the Issuer II Class C Units in TRC. The primary source of funds to make payments on the Non-Recourse 2035 Notes is the 63.75% economic interest of the Issuer (evidenced by the Issuer II Class C Units) in any future payments that may be made by GSK to TRC under the strategic alliance agreement and under the portion of the collaboration agreement assigned to TRC by Innoviva (net of TRC expenses paid and the amount of cash, if any, expected to be used by TRC pursuant to the TRC LLC Agreement over the next four fiscal quarters) relating to the GSK-Partnered Respiratory Programs, including the TRELEGY program. As a result, the holders of the Non-Recourse 2035 Notes have no recourse against Theravance Biopharma even if the TRELEGY payments are insufficient to cover the principal and interest payments for the Non-Recourse 2035 Notes. Prior to and including the December 5, 2024 payment date, in the event that the distributions received by the Issuer II from TRC in a quarter is less than the interest accrued for that quarter, the principal amount of the Non-Recourse 2035 Notes will increase by the interest shortfall amount for that quarter. While the holders of the Non-Recourse 2035 Notes have no recourse against Theravance Biopharma, the terms of the Non-Recourse 2035 Notes also provide that Theravance Biopharma, at its option, may satisfy the quarterly interest payment obligations by making a capital contribution to the Issuer II.

A portion of the proceeds from the Non-Recourse 2035 Notes issuance were used to repay, in full, the remaining outstanding balance of the Non-Recourse 2033 Notes, as well as, a 5% premium on the early redemption of

the Non-Recourse 2033 Notes. The Non-Recourse 2033 Notes were issued in November 2018 and were structured similarly to the Non-Recourse 2035 Notes.

On June 29, 2021, we sold 6,700,000 ordinary shares at a price to the public of $15.00 per share (the "Shares"). Under the terms of the underwriting agreement, on June 29, 2021, the underwriters also exercised a 30-day option to purchase an additional 1,005,000 ordinary shares for a total of 7,705,000 ordinary shares sold. The total gross proceeds from the offering were $115.6 million, before deducting underwriting discounts and commissions and offering expenses. The Shares were issued pursuant to our currently effective shelf registration statement on Form S-3, which became effective automatically on December 3, 2019, and a prospectus supplement filed with the SEC in connection with the offering.

Corporate Restructuring

On September 15, 2021, we announced the Restructuring to focus our capital resources on our respiratory programs, resulting in an approximate 75% reduction in workforce to significantly reduce operational costs and preserve capital. Approximately 75% of the total reduction in workforce occurred at the end of November 2021, and the remainder will be completed at the end of February 2022. In 2021, we recognized $20.1 million of the Restructuring and related expenses comprised of $11.5 million in cash-related expenses and $8.6 million in non-cash expenses. We estimate that we will incur total Restructuring and related expenses of approximately $32.0 million comprised of $17.0 million in cash expenses associated with employee termination benefits and related costs and $15.0 million in non-cash expenses relating to the acceleration of equity-awards for employees affected by the Restructuring and certain related awards for other employees. We expect to recognize the majority of the remaining approximate $12.0 million in Restructuring and related expenses, comprised of $5.0 million in cash-related expenses and $7.0 million in non-cash expenses, in the first quarter of 2022 and the balance by the third quarter of 2022.

As a result of the Restructuring, we expect to realize estimated operating expense savings (excluding share-based compensation and any one-time restructuring, severance, and termination costs) of approximately $170.0 million. We expect to be sustainably cash flow positive beginning in the second half of 2022 primarily achieved through our reduced cash expenditures in light of the Restructuring and the focus on our respiratory assets. These estimates are subject to a number of assumptions, and actual results may differ. We may also incur additional costs not currently contemplated due to events that may occur because of, or that are associated with, the Restructuring.

Despite expected expense savings from the Restructuring, we may continue to incur net losses over the next several years due to expenditures relating to our continuing respiratory drug discovery efforts and preclinical and clinical development of our current respiratory product candidates. In particular, to the extent we advance our respiratory product candidates into and through later-stage clinical studies without a partner, we may incur substantial expenses. In addition, we may invest strategically in our research efforts to continue to grow our respiratory development pipeline. In the past, we have received a number of significant payments from collaboration agreements and other significant transactions. In the future, we may continue to receive potential substantial payments from future collaboration transactions if the drug candidates in our pipeline achieve positive clinical or regulatory outcomes or if our product candidates are approved and meet certain milestones.

Our new strategic business plan is subject to significant uncertainties and risks as a result of, among other factors, the COVID-19 pandemic, clinical program outcomes, whether, when and on what terms we are able to enter into new collaboration arrangements, expenses being higher than anticipated, the sales levels of our approved products, unplanned expenses, cash receipts being lower than anticipated, and the need to satisfy contingent liabilities, including litigation matters and indemnification obligations.

Adequacy of cash resources to meet future needs

We expect our cash, cash equivalents and marketable securities will be sufficient to fund our operations for at least the next twelve months from the date of issuance of this Annual Report on Form 10-K based on current operating plans and financial forecasts. We plan to be sustainably cash flow positive beginning in the second half of 2022 primarily driven by our Restructuring and forecasted revenues and royalties generated by YUPELRI and TRELEGY net sales.

As needed, we may seek to obtain additional financing in the form of public or private equity offerings, debt financing or additional collaborations and licensing arrangements. However, future financing may not be available in amounts or on terms acceptable to us.

Without adequate financial resources to fund our expected future operations, we may be required to relinquish rights to our technologies, product candidates or territories, or grant licenses on terms that are not favorable to us, in order to raise additional funds through collaborations or licensing arrangements. We may also have to sequence preclinical and clinical studies as opposed to conducting them concomitantly in order to conserve resources, or, as we have recently announced in September 2021, we may need to delay, reduce or eliminate one or more of our research or development programs and reduce overall overhead expenses. In addition, we may have to make further reductions in our workforce and may be prevented from continuing our discovery, development and commercialization efforts and exploiting other corporate opportunities.

Cash Flows

Cash flows, as compared to the prior years, were as follows:

	Year Ended December 31,			Change	
(In thousands)	**2021**	**2020**	**2019**	**2020**	**2019**
Net cash used in operating activities	$ (207,858)	$ (250,403)	$ (238,197)	$ 42,545	$ (12,206)
Net cash provided by (used in) investing activities	124,494	10,721	(83,051)	113,773	93,772
Net cash provided by financing activities	91,860	263,085	1,291	(171,225)	261,794

Net cash flows used in operating activities

Net cash used in operating activities was $207.9 million in 2021, consisting of a net loss of $199.4 million, a net increase in cash resulting from adjustments for non-cash and other reconciling items of $31.2 million and a net decrease in cash resulting from changes in operating assets and liabilities of $39.6 million.

Net cash used in operating activities was $250.4 million in 2020, consisting primarily of a net loss of $278.0 million, a net increase in cash resulting from adjustments for total non-cash and other reconciling items of $67.1 million and a net decrease in cash resulting from changes in operating assets and liabilities of $39.5 million.

Net cash flows provided by (used in) investing activities

Net cash provided by investing activities was $124.5 million in 2021, consisting primarily of cash inflows from the net purchase and maturities of marketable securities of $127.9 million and partially offset by $3.4 million used for the purchase of property and equipment.

Net cash provided by investing activities was $10.7 million in 2020 and was primarily attributed the proceeds from the sales of marketable securities of $19.9 million which was partially offset by $6.6 million related to the purchase of property and equipment and $2.7 million in cash outflows resulting from net purchases and maturities of marketable securities.

Net cash flows provided by financing activities

Net cash provided by financing activities was $91.9 million in 2021, consisting of the sale of 7,705,000 ordinary shares for total net proceeds of $108.2 million and $3.5 million in proceeds from ESPP and share option purchases. These proceeds were partially offset by $10.7 million in principal payments on the Non-Recourse 2035 Notes and $9.1 million related to the repurchase of shares to satisfy tax withholding obligations.

Net cash provided by financing activities was $263.1 million in 2020, consisting primarily of the sale of 5,500,000 ordinary shares for total net proceeds of $139.9 million and the issuance of our Non-Recourse 2035 Notes for

total net proceeds of $374.7 million. A portion of the of the Non-Recourse 2035 Notes proceeds were used to repay, in full, the remaining $235.3 million outstanding balance of our Non-Recourse 2033 Notes and an $11.5 million redemption premium related to the payoff of the Non-Recourse 2033 Notes. In addition to the above, net cash provided by financing activities was partially offset by the repurchase of shares to satisfy tax withholding obligations in the amount of $9.7 million.

Contractual Obligations

In the table below, we set forth our significant contractual obligations, as well as obligations related to contracts that we are likely to continue, regardless of the fact that some were cancelable as of December 31, 2021. Some of the amounts that we include in this table are based on management's estimate and assumptions about these obligations, including their duration. Because these estimates and assumptions are necessarily subjective, the amount of the obligations that we will pay in future periods may vary from those reflected in the table.

		Years			
(In thousands)	**Total**	**Within 1**	**1 to 3**	**3 to 5**	**After 5**
3.25% Convertible senior notes due 2023 - principal	$ 230,000	$ —	$ 230,000	$ —	$ —
3.25% Convertible senior notes due 2023 - interest	13,725	7,475	6,250	—	—
9.5% Non-recourse notes due 2035 - net principal *	392,626	*	*	*	*
Facility operating leases	85,847	9,312	19,425	20,558	36,552
Purchase obligations (1)	54,632	52,773	1,859	—	—
Total	$ 776,830	$ 69,560	$ 257,534	$ 20,558	$ 36,552

* The Non-Recourse 2035 Notes are secured by the Issuer II's right, title, and interest in TRC. The primary source of funds to make payments on the Non-Recourse 2035 Notes is the 63.75% economic interest of the Issuer II in any future payments made by GSK under the collaboration agreement, dated as of November 14, 2002, by and between Innoviva and GSK relating to the TRELEGY program. In addition, prior to December 5, 2024, in the event that the distributions received by the Issuer II from TRC in a quarter is less than the interest accrued for the quarter, the principal amount of the Non-Recourse 2035 Notes will increase by the interest shortfall amount for that period. Since the timing of the principal and interest payments on the Non-Recourse 2035 Notes is ultimately based on royalties from TRELEGY product sales, which will vary from quarter to quarter and are unknown to us, only the total net principal payment amount at issuance is included in the above table. See "*Item 8, Note 6. Debt*" of the accompanying consolidated financial statements for further information.

(1) Substantially all of this amount was comprised of open purchase orders, as of December 31, 2021, that were issued under existing contracts. This amount does not represent any minimum contract termination liabilities related to our existing contracts.

Commitments and Contingencies

We indemnify our officers and directors for certain events or occurrences, subject to certain limits. We maintain insurance policies that may limit our exposure, and therefore, we believe the fair value of these indemnification agreements is minimal. Accordingly, we have not recognized any liabilities relating to these agreements as of December 31, 2021. However, no assurances can be given regarding the amounts that may ultimately be covered by the insurers, and we may incur substantial liabilities because of these indemnification obligations.

Performance-Contingent Awards

We periodically grant performance-contingent awards to our employees. For the year ended December 31, 2021, we recognized $0.8 million of aggregate share-based compensation expense and $0.4 million in cash bonus expense related to these types of awards. As of December 31, 2021, the maximum remaining expense related to

outstanding performance-contingent awards was $2.9 million which had performance expiration dates through December 2025.

Recent Accounting Pronouncements

The information required by this item is included in *"Item 8, Note 1. Organization and Summary of Significant Accounting Policies,"* in our consolidated financial statements included in this Annual Report on Form 10-K.

ITEM 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

We are exposed to market risks in the ordinary course of our business. These risks primarily include risk related to interest rate sensitivities.

Interest Rate Sensitivity

We have invested primarily in money market funds, federal agency notes, corporate debt securities, commercial papers and US treasury notes. To reduce the volatility relating to these exposures, we have put investment and risk management policies and procedures in place. The securities in our investment portfolio are not leveraged and are classified as available-for-sale due to their short-term nature. We currently do not engage in hedging activities.

We performed a sensitivity analysis to determine the impact a change in interest rates would have on the value of our investment portfolio. As of December 31, 2021 and 2020, we have estimated that a hypothetical 100 basis point increase in interest rates would have resulted in a decrease in the fair market value of our investment portfolio of $0.2 million and $0.5 million, respectively. Such losses would only be realized if we sold the investments prior to maturity.

We are also subject to interest rate sensitivity on our outstanding Convertible Senior 2023 Notes that were issued in November 2016 and our Non-Recourse 2035 Notes that were issued in February 2020. Increases in interest rates would result in a decrease in the fair value of our outstanding debt and decreases in interest rates would result in an increase in the fair value of our outstanding debt. These decreases or increases in the fair value of our outstanding debt would be partially offset by corresponding decreases or increases in our fixed income investment portfolio. The Convertible Senior 2023 Notes pay interest semi-annually, and the $230.0 million of principal is scheduled to be repaid in October 2023. The Non-Recourse 2035 Notes pay interest and principal quarterly, and the remaining net principal of $392.6 million is due by 2035.

ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA

Report of Independent Registered Public Accounting Firm

To the Shareholders and Board of Directors of Theravance Biopharma, Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Theravance Biopharma, Inc. (the "Company") as of December 31, 2021 and 2020, the related consolidated statements of operations, comprehensive loss, shareholders' deficit, and cash flows for each of the three years in the period ended December 31, 2021, and the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, based on our audits and the report of other auditors, the consolidated financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2021 and 2020, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2021, in conformity with U.S. generally accepted accounting principles.

We did not audit the financial statements of Theravance Respiratory Company, LLC ("TRC"), an entity in which the Company has an 85% economic interest. The Company's equity in net assets of TRC and amounts due from TRC totaled $111.1 million at December 31, 2021, and the Company's equity in the net income of TRC was $104.0 million for 2021. The 2021 financial statements of TRC were audited by other auditors whose report has been furnished to us, and our opinion, insofar as it relates to the 2021 amounts included for TRC, is based solely on the report of the other auditors.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) ("PCAOB"), Theravance Biopharma, Inc.'s internal control over financial reporting as of December 31, 2021, based on criteria established in Internal Control-Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework) and our report dated February 28, 2022 expressed an unqualified opinion thereon.

Basis for Opinion

These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's financial statements based on our audits. We are a public accounting firm registered with the PCAOB and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits and the report of other auditors provide a reasonable basis for our opinion.

Critical Audit Matter

The critical audit matter communicated below is a matter arising from the current period audit of the financial statements that was communicated or required to be communicated to the audit committee and that: (1) relates to accounts or disclosures that are material to the financial statements and (2) involved our especially challenging, subjective or complex judgments. The communication of the critical audit matter does not alter in any way our opinion on the consolidated financial statements, taken as a whole, and we are not, by communicating the critical audit matter below, providing a separate opinion on the critical audit matter or on the accounts or disclosures to which it relates.

Revenue from collaborative and licensing arrangements

Description of the Matter

The Company recognized revenue from its Janssen Biotech, Inc. collaboration and licensing agreement (the "Janssen Agreement") of $11.4 million for the year ended December 31, 2021. As described in Note 1, collaboration agreements may include many elements such as up-front fees, milestones, royalties, expense reimbursement, and/or profit sharing. Furthermore, collaborations may include the delivery of various goods or services to the collaborative partner such as licenses to intellectual property or research and development services. In some circumstances, management is required to use judgment to determine whether analogies to the revenue accounting literature are appropriate for elements of collaboration arrangements. Revenue recognized under the Janssen Agreement is based on a measure of the Company's efforts toward satisfying the performance obligation relative to the total expected efforts or inputs to satisfy the performance obligation (e.g., costs incurred compared to total budget).

Auditing the Company's accounting for revenues from collaboration arrangements was especially challenging due to the complex and highly judgmental nature of evaluating the terms of the related agreements, identifying performance obligations, evaluating whether analogies to the revenue accounting guidance are appropriate, determining and allocating the transaction price to the performance obligations, evaluating estimates of the expected efforts to complete performance obligations and measuring efforts toward satisfying those performance obligations, especially as such measuring of efforts relates to the Janssen Agreement.

How We Addressed the Matter in Our Audit

We obtained an understanding, evaluated the design, and tested the operating effectiveness of controls over the Company's processes for assessing the accounting treatment of any new collaboration agreements or modifications to existing collaboration agreements, establishing an estimated budget of costs, assessing the effort to satisfy performance obligations, and recording actual costs incurred including controls over the completeness and accuracy of data used in the underlying analysis.

To test the accounting for revenue from collaboration arrangements we tested and evaluated, among other things, the performance obligations identified, the estimates and assumptions used to determine transaction price, and the allocation of transaction price to performance obligations. We assessed whether management's analogies to the revenue literature were a consistent and rational application of accounting policy. To test the measurement of efforts toward satisfying performance obligations, our audit procedures included, among others, reviewing management's analysis for accuracy and completeness by agreeing data to underlying agreements and inspecting communications with collaboration partners. As of December 31, 2021, we obtained the formal termination letter issued by Janssen to the Company, which supported completion of the Company's performance obligation under the arrangement and that the remaining deferred allocated transaction price was appropriately recognized as revenue.

/s/ Ernst & Young LLP

We have served as the Company's auditor since 2013.
Redwood City, California
February 28, 2022

THERAVANCE BIOPHARMA, INC.
CONSOLIDATED BALANCE SHEETS
(In thousands, except per share data)

	December 31, 2021	December 31, 2020
Assets		
Current assets:		
Cash and cash equivalents	$ 89,959	$ 81,467
Short-term marketable securities	83,506	211,474
Receivables from collaborative arrangements	14,065	15,868
Amounts due from TRC, LLC	43,534	53,799
Prepaid clinical and development services	10,245	20,374
Other prepaid and current assets	8,561	10,359
Total current assets	249,870	393,341
Property and equipment, net	13,657	16,422
Operating lease assets	39,690	43,260
Equity in net assets of TRC, LLC	67,537	12,750
Restricted cash	837	833
Other assets	3,228	2,451
Total assets	$ 374,819	$ 469,057
Liabilities and Shareholders' Deficit		
Current liabilities:		
Accounts payable	$ 3,098	$ 6,775
Accrued personnel-related expenses	12,796	35,238
Accrued clinical and development expenses	17,010	28,799
Accrued general and administrative expenses	2,898	6,048
Accrued interest payable	3,940	3,974
Current portion of non-recourse notes due 2035, net	16,940	19,334
Operating lease liabilities	503	9,867
Deferred revenue	98	11,523
Other accrued liabilities	1,304	2,013
Total current liabilities	58,587	123,571
Convertible senior notes due 2023, net	228,035	226,963
Non-recourse notes due 2035, net	371,359	372,873
Long-term operating lease liabilities	52,681	47,220
Long-term deferred revenue	310	348
Other long-term liabilities	2,420	1,833
Commitments and contingencies		
Shareholders' Deficit		
Preferred shares, $0.00001 par value: 230 shares authorized, no shares issued or outstanding	—	—
Ordinary shares, $0.00001 par value: 200,000 shares authorized; 74,435 and 64,328 shares issued and outstanding at December 31, 2021 and December 31, 2020, respectively	1	1
Additional paid-in capital	1,387,469	1,222,818
Accumulated other comprehensive income	—	47
Accumulated deficit	(1,726,043)	(1,526,617)
Total shareholders' deficit	(338,573)	(303,751)
Total liabilities and shareholders' deficit	$ 374,819	$ 469,057

See accompanying notes to consolidated financial statements

THERAVANCE BIOPHARMA, INC.
CONSOLIDATED STATEMENTS OF OPERATIONS
(In thousands, except per share data)

	Year Ended December 31,		
	2021	2020	2019
Revenue:			
Collaboration revenue	$ 11,463	$ 26,464	$ 31,250
Licensing revenue	—	1,500	28,500
Viatris collaboration agreement	43,848	43,893	13,664
Total revenue	55,311	71,857	73,414
Expenses:			
Research and development (1)	193,657	260,953	219,248
Selling, general and administrative (1)	99,296	108,661	106,081
Restructuring and related expenses (1)	20,142	—	—
Total expenses	313,095	369,614	325,329
Loss from operations	(257,784)	(297,757)	(251,915)
Income from investment in TRC, LLC	103,987	68,438	33,705
Interest expense	(46,889)	(44,585)	(31,862)
Loss on extinguishment of debt	—	(15,464)	—
Interest and other income, net	1,109	2,831	8,395
Loss before income taxes	(199,577)	(286,537)	(241,677)
Provision for income tax benefit	151	8,520	5,222
Net loss	$ (199,426)	$ (278,017)	$ (236,455)
Net loss per share:			
Basic and diluted net loss per share	$ (2.87)	$ (4.46)	$ (4.25)
Shares used to compute basic and diluted net loss per share	69,461	62,345	55,610

(1) Amounts include share-based compensation expense as follows:

	Year Ended December 31,		
(In thousands)	2021	2020	2019
Research and development	$ 25,634	$ 31,294	$ 28,953
Selling, general and administrative	28,065	31,682	31,497
Restructuring and related expenses	8,362	—	—
Total share-based compensation expense	$ 62,061	$ 62,976	$ 60,450

See accompanying notes to consolidated financial statements.

THERAVANCE BIOPHARMA, INC.
CONSOLIDATED STATEMENTS OF COMPREHENSIVE LOSS
(In thousands)

	Year Ended December 31,		
	2021	2020	2019
Net loss	$ (199,426)	$ (278,017)	$ (236,455)
Other comprehensive income (loss):			
Net unrealized gain (loss) on available-for-sale investments, net of tax	(47)	(98)	311
Comprehensive loss	$ (199,473)	$ (278,115)	$ (236,144)

See accompanying notes to consolidated financial statements.

THERAVANCE BIOPHARMA, INC.
CONSOLIDATED STATEMENTS OF SHAREHOLDERS' DEFICIT
(In thousands)

	Ordinary Shares		Additional Paid-In Capital	Accumulated Other Comprehensive Income (Loss)	Accumulated Deficit	Total Shareholders' Deficit
	Shares	Amount				
Balances at December 31, 2018	55,681	$ 1	$ 960,721	$ (166)	$ (1,012,145)	$ (51,589)
Proceeds from ESPP purchases	203	—	3,474	—	—	3,474
Employee share-based compensation expense	—	—	60,450	—	—	60,450
Issuance of restricted shares	1,105	—	—	—	—	—
Option exercises	164	—	3,142	—	—	3,142
Repurchase of shares to satisfy tax withholding	(138)	—	(3,173)	—	—	(3,173)
Net unrealized gain on marketable securities	—	—	—	311	—	311
Net loss	—	—	—	—	(236,455)	(236,455)
Balances at December 31, 2019	57,015	$ 1	$ 1,024,614	$ 145	$ (1,248,600)	$ (223,840)

	Ordinary Shares		Additional Paid-In Capital	Accumulated Other Comprehensive Income (Loss)	Accumulated Deficit	Total Shareholders' Deficit
	Shares	Amount				
Balances at December 31, 2019	57,015	$ 1	$ 1,024,614	$ 145	$ (1,248,600)	$ (223,840)
Net proceeds from sale of ordinary shares	5,500	—	139,915	—	—	139,915
Proceeds from ESPP purchases	245	—	3,701	—	—	3,701
Employee share-based compensation expense	—	—	62,976	—	—	62,976
Issuance of restricted shares	1,907	—	—	—	—	—
Option exercises	68	—	1,361	—	—	1,361
Repurchase of shares to satisfy tax withholding	(407)	—	(9,749)	—	—	(9,749)
Net unrealized loss on marketable securities	—	—	—	(98)	—	(98)
Net loss	—	—	—	—	(278,017)	(278,017)
Balances at December 31, 2020	64,328	$ 1	$ 1,222,818	$ 47	$ (1,526,617)	$ (303,751)

	Ordinary Shares		Additional Paid-In Capital	Accumulated Other Comprehensive Income (Loss)	Accumulated Deficit	Total Shareholders' Deficit
	Shares	Amount				
Balances at December 31, 2020	64,328	$ 1	$ 1,222,818	$ 47	$ (1,526,617)	$ (303,751)
Net proceeds from sale of ordinary shares	7,705	—	108,180	—	—	108,180
Proceeds from ESPP purchases	275	—	3,466	—	—	3,466
Employee share-based compensation expense	—	—	62,061	—	—	62,061
Issuance of restricted shares	2,682	—	—	—	—	—
Option exercises	—	—	5	—	—	5
Repurchase of shares to satisfy tax withholding	(555)	—	(9,061)	—	—	(9,061)
Net unrealized loss on marketable securities	—	—	—	(47)	—	(47)
Net loss	—	—	—	—	(199,426)	(199,426)
Balances at December 31, 2021	74,435	$ 1	$ 1,387,469	$ —	$ (1,726,043)	$ (338,573)

See accompanying notes to consolidated financial statements.

THERAVANCE BIOPHARMA, INC.
CONSOLIDATED STATEMENTS OF CASH FLOWS
(In thousands)

	Year Ended December 31,		
	2021	2020	2019
Operating activities			
Net loss	$ (199,426)	$ (278,017)	$ (236,455)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization	5,912	6,798	6,441
Amortization and accretion income, net	10	(1,079)	(3,451)
Share-based compensation	62,061	62,976	60,450
Loss on disposal of property and equipment	39	—	—
Amortization of right-of-use assets	3,786	3,344	3,224
Gain from lease modification	(1,863)	—	—
Undistributed earnings from TRC, LLC	(44,516)	(37,975)	(23,152)
Interest shortfall on 2035 notes, net	5,713	17,643	—
Loss on extinguishment of debt	—	15,464	—
Other	10	(95)	146
Changes in operating assets and liabilities:			
Accounts receivable	—	—	620
Receivables from collaborative and licensing arrangements	1,803	6,128	(11,943)
Prepaid clinical and development services	10,129	(17,638)	(561)
Other prepaid and current assets	2,867	(2,327)	(73)
Tax receivable	—	(258)	(3,700)
Other assets	(972)	(852)	(358)
Accounts payable	(3,534)	3,658	(4,274)
Accrued personnel-related expenses, accrued clinical and development expenses, and other accrued liabilities	(37,225)	5,983	10,626
Accrued interest payable	(34)	(1,685)	2,573
Deferred revenue	(11,463)	(26,465)	(31,245)
Operating lease liabilities	(1,742)	1,600	(2,317)
Other long-term liabilities	587	(7,606)	(4,748)
Net cash used in operating activities	(207,858)	(250,403)	(238,197)
Investing activities			
Purchases of property and equipment	(3,406)	(6,616)	(3,176)
Purchases of marketable securities	(158,305)	(401,987)	(423,898)
Maturities of marketable securities	286,199	399,318	339,018
Proceeds from the sale of marketable securities	—	19,942	—
Proceeds from the sale of property and equipment	6	64	5
Proceeds from the sale of VIBATIV business, net	—	—	5,000
Net cash provided by (used in) investing activities	124,494	10,721	(83,051)
Financing activities			
Proceeds from the sale of ordinary shares, net	108,180	139,915	—
Proceeds from issuance of 2035 notes, net	—	380,000	—
Payment of issuance costs on 2035 notes	—	(5,326)	—
Principal payment on 2035 notes	(10,730)	—	—
Payment of redemption premium on 2033 notes	—	(11,470)	—
Principal payment on 2033 notes	—	(235,347)	(2,152)
Proceeds from ESPP purchases	3,466	3,701	3,474
Proceeds from option exercises	5	1,361	3,142
Repurchase of shares to satisfy tax withholding	(9,061)	(9,749)	(3,173)
Net cash provided by financing activities	91,860	263,085	1,291
Net increase (decrease) in cash, cash equivalents, and restricted cash	8,496	23,403	(319,957)
Cash, cash equivalents, and restricted cash at beginning of period	82,300	58,897	378,854
Cash, cash equivalents, and restricted cash at end of period	$ 90,796	$ 82,300	$ 58,897
Supplemental disclosure of cash flow information			
Cash paid for interest	$ 39,029	$ 24,024	$ 26,178
Cash (received) paid for income taxes, net	$ (4,089)	$ 14	$ 22
Right-of-use assets obtained in exchange for lease obligations (1)	$ —	$ —	$ 49,847

(1) Amounts for the year ended December 31, 2019 include the transition adjustment for the adoption of ASC 842, *Leases*.

See accompanying notes to consolidated financial statements.

THERAVANCE BIOPHARMA, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

1. Organization and Summary of Significant Accounting Policies

Theravance Biopharma, Inc. (“Theravance Biopharma” or the “Company”) is a biopharmaceutical company primarily focused on the discovery, development and commercialization of respiratory medicines. The Company’s core purpose is to *create medicines that make a difference*® in people’s lives.

Basis of Presentation

The Company’s consolidated financial statements as of December 31, 2021 and 2020, and for the year ended December 31, 2021, 2020, and 2019 have been prepared in conformity with United States (“US”) Generally Accepted Accounting Principles ("GAAP"), and the US Securities and Exchange (“SEC”) regulations for annual reporting.

Principles of Consolidation

The consolidated financial statements include the accounts of Theravance Biopharma and its wholly-owned subsidiaries, all of which are denominated in US dollars. All intercompany balances and transactions have been eliminated in consolidation.

Use of Estimates

The preparation of financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the reported amounts of assets, liabilities, revenues and expenses, and related disclosures in the consolidated financial statements and accompanying notes. Management bases its estimates on historical experience and on assumptions believed to be reasonable under the circumstances. Actual results could differ materially from those estimates.

Segment Reporting

The Company operates in a single segment, which is the discovery (research), development and commercialization of human therapeutics. The Company’s business offerings have similar economics and other characteristics, including the nature of products and manufacturing processes, types of customers, distribution methods and regulatory environment. The Company is comprehensively managed as one business segment by the Company’s Chief Executive Officer and the management team. Revenue from collaborative arrangements, including royalty revenue, are attributed to regions based on the location of the collaboration partner. Revenue from profit sharing-type arrangements is attributed to the geographic market in which the products are sold. Capitalized property and equipment is predominantly located in the US.

Cash and Cash Equivalents

The Company considers all highly-liquid investments purchased with a maturity of three months or less on the date of purchase to be cash equivalents. Cash equivalents are carried at fair value.

Restricted Cash

The Company maintains restricted cash for certain lease agreements and letters of credit by which the Company has pledged cash and cash equivalents as collateral. The Company may also maintain restricted cash for debt servicing of its non-recourse notes. See *“Note 4. Cash, Cash Equivalents, and Restricted Cash”* for more information.

Investments in Marketable Securities

The Company invests in marketable securities, primarily commercial paper, corporate notes, government bonds and government agency bonds. The Company classifies its marketable securities as available-for-sale securities and reports them at fair value in cash and cash equivalents or marketable securities on the consolidated balance sheets with related unrealized gains and losses included as a component of shareholders’ deficit. The amortized cost of debt

securities is adjusted for amortization of premiums and accretion of discounts to maturity, which is included in interest and other income (loss) on the consolidated statements of operations. The cost of securities sold is based on the specific identification method. Realized gains and losses and interest and dividends on securities are included in interest and other income (loss).

The Company accounts for credit losses on available-for-sale debt securities in accordance with Accounting Standards Codification ("ASC"), Topic 326, *Financial Instruments – Credit Losses* ("ASC 326"). Under ASC 326, the Company regularly reviews its investments for declines in estimated fair value below amortized cost. The factors considered in determining whether a credit loss exists include the creditworthiness of the security issuers, the number of securities in unrealized loss positions, the severity and duration of the unrealized losses, whether the Company has the intent to sell the securities and whether it is more likely than not that the Company will be required to sell the securities before the recovery of the security's amortized cost basis.

In circumstances where the Company intends to sell, or is more likely than not required to sell, the security before it recovers its amortized cost basis, the difference between fair value and amortized cost is recognized as a loss in the consolidated statements of operations, with a corresponding write-down of the security's amortized cost. In circumstances where neither condition exists, the Company then evaluates whether a decline is due to credit-related factors. To determine the portion of a decline in fair value that is credit-related, the Company compares the present value of the expected cash flows of the security discounted at the security's effective interest rate to the amortized cost basis of the security. A credit-related impairment is limited to the difference between fair value and amortized cost and recognized as an allowance for credit loss on the consolidated balance sheets with a corresponding adjustment to net income (loss). Any remaining decline in fair value that is non-credit related is recognized in other comprehensive loss, net of tax. Improvements in expected cash flows due to improvements in credit are recognized through reversal of the credit loss and corresponding reduction in the allowance for credit loss.

Fair Value of Financial Instruments

The Company defines fair value as the exchange price that would be received for an asset or paid to transfer a liability (an exit price) in the principal or most advantageous market for the asset or liability in an orderly transaction between market participants on the measurement date.

The Company's valuation techniques are based on observable and unobservable inputs. Observable inputs reflect readily obtainable data from independent sources, while unobservable inputs reflect the Company's market assumptions. The Company classifies these inputs into the following hierarchy:

Level 1 — Quoted prices for identical instruments in active markets.

Level 2 — Quoted prices for similar instruments in active markets; quoted prices for identical or similar instruments in markets that are not active; and model-derived valuations whose inputs are observable or whose significant value drivers are observable.

Level 3 — Unobservable inputs and little, if any, market activity for the assets.

Financial instruments include cash equivalents, marketable securities, accounts receivable, accounts payable, accrued liabilities and debt. The Company's cash equivalents and marketable securities are carried at estimated fair value and remeasured on a recurring basis. The carrying value of accounts receivable, receivables from collaborative arrangements, accounts payable and accrued liabilities approximate their estimated fair value due to the relatively short-term nature of these instruments. The fair value of the Company's debt is classified as a level 2 financial instrument and is disclosed in *"Note 6. Debt"*.

Receivables from Collaborative Arrangements

For the periods presented, the Company's receivables from collaborative arrangements relate to amounts due arising from its collaboration (and licensing) agreements. When appropriate, the Company provides for an allowance for credit losses. The Company performs periodic credit evaluations of its customers and generally does not require

collateral. For the periods presented, the Company did not have any material write-offs of receivables from collaborative arrangements.

Concentration of Credit Risks

The Company invests in a variety of financial instruments and, based on its policy, limits the amount of credit exposure with any one issuer, industry or geographic area for investments other than instruments backed by the US federal government.

The Company's receivables primarily relate to amounts due under its collaboration and licensing agreements. Accordingly, the Company may be exposed to credit risk generally associated with pharmaceutical companies or specific to its collaboration agreements. The Company performs periodic evaluations of its customers and generally does not require collateral. For the year ended December 31, 2021, 2020, and 2019, the Company did not experience any material losses related to its receivables.

Property and Equipment

Property, equipment and leasehold improvements are stated at cost, net of accumulated depreciation, and amortized using the straight-line method as follows:

Leasehold improvements	Shorter of remaining lease terms or useful life
Equipment, furniture and fixtures	5 - 7 years
Software and computer equipment	3 - 5 years

Leases

The Company determines whether a contract is or contains a lease at inception of the arrangement. In evaluating whether a contract is indicative of a lease, the Company considers all relevant facts and circumstances to assess whether the arrangement has extended to the Company the right to both (i) obtain substantially all the economic benefits from use of an identified asset and (ii) direct the use of the identified asset. To the extent that the Company determines a contract represents a lease, the arrangement is classified as either an operating lease or a finance lease, with the classification affecting the presentation and pattern of expense recognition in the consolidated statements of operations. The Company did not have any finance leases at either December 31, 2021 or 2020.

Operating lease assets represent the Company's right to use an underlying asset for the lease term and operating lease liabilities represent the Company's obligation to make lease payments arising from the leasing arrangement. The Company records operating leases on the consolidated balance sheets through an operating lease asset and a corresponding short-term and long-term operating lease liability, as applicable. Lease liabilities are measured based on the present value of lease payments over the lease term discounted at the implicit interest rate, when readily available or using the Company's incremental borrowing rate, if the implicit rate is not determinable. The incremental borrowing rate is considered the rate of interest that the Company would have to pay to borrow, on a collateralized basis over a similar term, an amount equal to the lease payments in a similar economic environment. The Company measures its operating lease assets based on the corresponding operating lease liabilities adjusted for (i) prepayments made to the lessor at or before the commencement date, (ii) any initial direct costs incurred, and (iii) tenant incentives granted under the lease contract.

In calculating operating lease assets and liabilities, the Company may elect to combine lease and non-lease components based on the asset type. The Company's lease terms may include options to extend the lease only when it is reasonably certain that such options will be exercised, and the Company recognizes lease expense on a straight-line basis over the lease term. Operating lease assets are evaluated for possible impairment in accordance with the Company's long-lived assets policy.

The Company does not recognize operating lease assets or liabilities for leases that have a lease term of 12 months or less at commencement date, and the lease expense related to these short-term lease arrangements is recognized on a straight-line basis over the term of the lease.

Capitalized Software

The Company capitalizes certain costs related to direct material and service costs for software obtained for internal use. Upon being placed in service, these costs and other future capitalizable costs related to the internal use software system integration are depreciated over five years. There were no material capitalized software costs recorded for the year ended December 31, 2021 or 2020.

Impairment of Long-Lived Assets

The Company's long-lived assets consists of property and equipment, operating lease assets and other assets. The carrying value of long-lived assets is reviewed for impairment whenever events or changes in circumstances indicate that the asset may not be recoverable. An impairment loss is recognized when the total of estimated future cash flows expected to result from the use of the asset and its eventual disposition is less than its carrying amount. There was no impairment of long-lived assets recorded for the year ended December 31, 2021, 2020, or 2019.

Revenue Recognition

The Company recognizes revenue under ASC Topic 606, *Revenue from Contracts with Customers* ("ASC 606"). Under ASC 606, an entity recognizes revenue when its customer obtains control of promised goods or services, in an amount that reflects the consideration which the entity expects to receive in exchange for those goods or services. To determine revenue recognition for arrangements that an entity determines are within the scope of ASC 606, an entity performs the following five steps: (i) identify the contract(s) with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when (or as) the entity satisfies a performance obligation.

At contract inception, once the contract is determined to be within the scope of ASC 606, the Company identifies the performance obligations in the contract by assessing whether the goods or services promised within each contract are distinct. The Company then recognizes revenue for the amount of the transaction price that is allocated to the respective performance obligation when (or as) the performance obligation is satisfied.

Collaborative Arrangements under ASC 606

The Company enters into collaborative arrangements with partners that fall under the scope of ASC Topic 808, *Collaborative Arrangements* ("ASC 808"). While these arrangements are in the scope of ASC 808, the Company may analogize to ASC 606 for some aspects of these arrangements. The Company analogizes to ASC 606 for certain activities within collaborative arrangements for the delivery of a good or service (i.e., a unit of account) that is part of its ongoing major or central operations. Revenue recognized by analogizing to ASC 606 is recorded as "collaboration revenue" or "licensing revenue" whereas, revenue recognized in accordance with ASC 808 is recorded on a separate collaboration revenue line on the consolidated statements of operations.

The terms of the Company's collaborative arrangements typically include one or more of the following: (i) up-front fees; (ii) milestone payments related to the achievement of development, regulatory, or commercial goals; (iii) royalties on net sales of licensed products; (iv) reimbursements or cost-sharing of research and development expenses; and (v) profit/loss sharing arising from co-promotion arrangements. Each of these payments results in collaboration revenues or an offset against research and development expense. Where a portion of non-refundable up-front fees or other payments received is allocated to continuing performance obligations under the terms of a collaborative arrangement, they are recorded as deferred revenue and recognized as collaboration revenue when (or as) the underlying performance obligation is satisfied.

As part of the accounting for these arrangements, the Company must develop estimates and assumptions that require judgment to determine the underlying stand-alone selling price for each performance obligation which determines how the transaction price is allocated among the performance obligations. The estimation of the stand-alone selling price may include such estimates as, forecasted revenues or costs, development timelines, discount rates and probabilities of technical and regulatory success. The Company evaluates each performance obligation to determine if they can be satisfied at a point in time or over time, and it measures the services delivered to the collaborative partner which are periodically reviewed based on the progress of the related program. The effect of any change made to an

estimated input component and, therefore revenue or expense recognized, would be recorded as a change in estimate. In addition, variable consideration (e.g., milestone payments) must be evaluated to determine if it is constrained and, therefore, excluded from the transaction price.

Up-front Fees: If a license to the Company's intellectual property is determined to be distinct from the other performance obligations identified in the arrangement, the Company recognizes collaboration revenues from the transaction price allocated to the license when the license is transferred to the licensee and the licensee is able to use and benefit from the license. For licenses that are bundled with other promises, the Company utilizes judgment to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time and, if over time, the appropriate method of measuring progress for purposes of recognizing collaboration revenue from the allocated transaction price. For example, when the Company receives up-front fees for the performance of research and development services, or when research and development services are not considered to be distinct from a license, the Company recognizes collaboration revenue for those units of account over time using a measure of progress. The Company evaluates the measure of progress each reporting period and, if necessary, adjusts the measure of performance and related revenue or expense recognition as a change in estimate.

Milestone Payments: At the inception of each arrangement that includes milestone payments (variable consideration), the Company evaluates whether the milestones are considered probable of being reached and estimates the amount to be included in the transaction price using the most likely amount method. If it is probable that a significant revenue reversal would not occur, the associated milestone value is included in the transaction price. Milestone payments that are not within the Company's or the collaborative partner's control, such as non-operational developmental and regulatory approvals, are generally not considered probable of being achieved until those approvals are received. At the end of each reporting period, the Company re-evaluates the probability of achievement of milestones that are within its or the collaborative partner's control, such as operational developmental milestones and any related constraint, and if necessary, adjusts its estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis, which would affect collaboration revenues and earnings in the period of adjustment. Revisions to the Company's estimate of the transaction price may also result in negative collaboration revenues and earnings in the period of adjustment.

Royalties: For arrangements that include sales-based royalties, including commercial milestone payments based on the level of sales, and the license is deemed to be the predominant item to which the royalties relate, the Company recognizes revenue at the later of (i) when the related sales occur, or (ii) when the performance obligation to which some or all of the royalty has been allocated has been satisfied (or partially satisfied). The Company's income earned related to TRELEGY sales is included within "income from investment in TRC, LLC" on the consolidated statements of operations.

Reimbursement, cost-sharing and profit-sharing payments: Under certain collaborative arrangements, the Company has been reimbursed for a portion of its research and development expenses or participates in the cost-sharing of such research and development expenses. Such reimbursements and cost-sharing arrangements have been reflected as a reduction of research and development expense in the Company's consolidated statements of operations, as the Company does not consider performing research and development services for reimbursement to be a part of its ongoing major or central operations.

Research and Development Expenses

Research and development ("R&D") expenses are recorded in the period that services are rendered or goods are received. R&D expenses consist of salaries and benefits, laboratory supplies and facility costs, as well as fees paid to third parties that conduct certain R&D activities on behalf of the Company, net of certain external R&D expenses reimbursed under the Company's collaborative arrangements.

As part of the process of preparing its consolidated financial statements, the Company is required to estimate and accrue certain R&D expenses. This process involves the following:

- identifying services that have been performed on the Company's behalf and estimating the level of service performed and the associated cost incurred for the service when the Company has not yet been invoiced or otherwise notified of actual cost;
- estimating and accruing expenses in the Company's consolidated financial statements as of each balance sheet date based on facts and circumstances known to it at the time; and
- periodically confirming the accuracy of the Company's estimates with selected service providers and making adjustments, if necessary.

Examples of estimated R&D expenses that the Company accrues include:

- fees paid to clinical research organizations ("CROs") in connection with preclinical and toxicology studies and clinical studies;
- fees paid to investigative sites in connection with clinical studies;
- fees paid to contract manufacturing organizations ("CMOs") in connection with the production of product and clinical study materials; and
- professional service fees for consulting and related services.

The Company bases its expense accruals related to clinical studies on its estimates of the services received and efforts expended pursuant to contracts with multiple research institutions and CROs that conduct and manage clinical studies on the Company's behalf. The financial terms of these agreements vary from contract to contract and may result in uneven payment flows. Payments under some of these contracts depend on factors, such as the successful enrollment of patients and the completion of clinical study milestones. The Company's service providers typically invoice it monthly in arrears for services performed. In accruing service fees, the Company estimates the time period over which services will be performed and the level of effort to be expended in each period. If the Company does not identify costs that it has begun to incur or if it underestimates or overestimates the level of services performed or the costs of these services, the Company's actual expenses could differ from its estimates.

To date, the Company has not experienced significant changes in its estimates of accrued R&D expenses after a reporting period. However, due to the nature of estimates, there is no assurance that the Company will not make changes to its estimates in the future as it becomes aware of additional information about the status or conduct of its clinical studies and other R&D activities. Such changes in estimates will be recognized as R&D expenses in the period that the change in estimate occurs.

Advertising Expenses

The Company expenses the costs of advertising, including promotional expenses, as incurred. Advertising expenses were $9.3 million, $6.3 million and $2.4 million for the year ended December 31, 2021, 2020, and 2019, respectively.

Fair Value of Share-Based Compensation Awards

The Company issues share-based awards to employees and non-employees, generally in the form of share options and restricted share units ("RSUs"). Share-based compensation expense is calculated based on awards ultimately expected to vest and is reduced for actual forfeitures as they occur. The Company expenses these share-based awards over the requisite service period on a straight-line basis, based on the grant date fair value of the awards.

The Company determines the fair value of RSUs using the closing market price of the Company's common shares on the day of grant. The Company uses the Black-Scholes-Merton option pricing model to estimate the fair value of options granted under its equity incentive plans and rights to acquire shares granted under its employee share purchase plan ("ESPP"). The Black-Scholes-Merton option pricing model requires the use of assumptions, including the expected term of the award and the expected share price volatility. The Company uses the "simplified" method as described in Staff Accounting Bulletin No. 107, *Share-Based Payment*, to estimate the expected option term.

The Company also issues performance share units that settle in the Company's shares. The fair value is determined on the date of the grant using the number of shares expected to be earned and the ending market value of the shares on grant date. The number of shares expected to vest is determined by assessing the probability that the performance criteria will be met and the associated targeted payout level that is forecasted will be achieved. For performance share units, the Company recognizes share-based compensation expense over the requisite service period using the accelerated attribution method when achievement of the performance criteria becomes probable.

Debt Instruments

Coupon interest on the Company's debt instruments is accrued using the effective interest rate method over the estimated period the debt will be repaid. Debt issuance costs are capitalized as deferred financing costs and presented as a reduction of the carrying value of the financial liability on the Company's consolidated balance sheets. Debt issuance costs subsequently are amortized to interest expense over the estimated life of the related debt based on the effective interest method. The Company considers whether there are any embedded features in its debt instruments that require bifurcation and separate accounting as derivative financial instruments pursuant to ASC Topic 815, *Derivatives and Hedging*. As of December 31, 2021 and 2020, the Company's debt instruments did not include any features that require bifurcation and separate derivative accounting.

Theravance Respiratory Company, LLC ("TRC")

Through the Company's 85% equity interest in TRC, the Company is entitled to receive an 85% economic interest in any future payments made by Glaxo Group or one of its affiliates ("GSK") under the strategic alliance agreement and under the portion of the collaboration agreement assigned to TRC (net of TRC expenses paid and the amount of cash, if any, expected to be used by TRC pursuant to the TRC LLC Agreement over the next four fiscal quarters). The primary drug program assigned to TRC is TRELEGY.

The Company analyzed its ownership, contractual and other interests in TRC to determine if TRC is a variable-interest entity ("VIE"), whether the Company has a variable interest in TRC and the nature and extent of that interest. The Company determined that TRC is a VIE. The party with the controlling financial interest, the primary beneficiary, is required to consolidate the entity determined to be a VIE. Therefore, the Company also assessed whether the Company is the primary beneficiary of TRC based on the power to direct its activities that most significantly impact its economic performance and the Company's obligation to absorb its losses or the right to receive benefits from it that could potentially be significant to TRC. Based on the Company's assessment, it determined that it is not the primary beneficiary of TRC, and, as a result, the Company does not consolidate TRC in its consolidated financial statements. TRC is recognized in the Company's consolidated financial statements under the equity method of accounting.

Income related to the Company's equity ownership of TRC is reflected within its consolidated statements of operations and is classified as non-operating income. Amounts due from TRC that we believe will be collected within one year and our equity in the net assets of TRC are reflected on our consolidated balance sheets as a current asset and a non-current asset, respectively. The portion of the Non-Recourse 2035 Notes classified as a current liability, if any, is based on the amount of royalties received, or receivable, as of December 31, 2021, that are expected to be collected from TRC and used to make a principal repayment on the Non-Recourse 2035 Notes within the next twelve months. The determination of the amounts likely to be received from TRC within the next twelve months requires significant judgement due to the significant variability of the amounts paid to the Company, as compared to the royalties due. Consequently, the actual amount paid to the holders of the 2035 Notes within twelve months of the reporting date may differ significantly from that recorded in the consolidated balance sheets.

Income Taxes

The Company utilizes the asset and liability method of accounting for income taxes. Under this method, deferred tax assets and liabilities are determined based on differences between financial reporting and tax basis of assets and liabilities and are measured using enacted tax rates and laws that are anticipated to be in effect when the differences are expected to reverse. A valuation allowance is provided when it is more likely than not that some portion or all of a deferred tax asset will not be realized.

The Company's total unrecognized tax benefits of $75.0 million and $63.4 million, as of December 31, 2021 and December 31, 2020, respectively, may reduce the effective tax rate in the period of recognition. The Company currently has a full valuation allowance against its deferred tax assets, which would impact the timing of the effective tax rate benefit should any of the Company's uncertain positions be favorably settled in the future.

The Company assesses all material positions, including all significant uncertain positions, in all tax years that are still subject to assessment or challenge by relevant taxing authorities. Assessing an uncertain tax position begins with the initial determination of the position's sustainability and is measured at the largest amount of benefit that is greater than 50% likely to be realized upon ultimate settlement. As of each balance sheet date, unresolved uncertain tax positions must be reassessed, and the Company will determine whether the factors underlying the sustainability assertion have changed and whether the amount of the recognized tax benefit is still appropriate.

The recognition and measurement of tax benefits requires significant judgment. The Company has taken certain positions where it believes that its position is greater than 50% likely to be realized upon ultimate settlement and for which no reserve for uncertain tax positions has been recorded. If the Company does not ultimately realize the expected benefit of these positions, it will record additional income tax expenses in future periods. Judgments concerning the recognition and measurement of a tax benefit might change as new information becomes available.

Any tax levied or credited by a governmental taxing authority that is not based on the Company's income is outside the scope of accounting for income taxes. Therefore, the Company records such items as a component of its loss before income taxes.

Net Loss per Share

Basic net loss per share is computed by dividing net loss by the weighted-average number of shares outstanding, less ordinary shares subject to forfeiture. Diluted net loss per share is computed by dividing net loss by the weighted-average number of shares outstanding, less ordinary shares subject to forfeiture, plus all additional ordinary shares that would have been outstanding, assuming dilutive potential ordinary shares had been issued for other dilutive securities.

	Year Ended December 31,		
(In thousands, except per share data)	**2021**	**2020**	**2019**
Numerator:			
Net loss	$ (199,426)	$ (278,017)	$ (236,455)
Denominator:			
Weighted-average ordinary shares outstanding	69,518	62,808	56,452
Less: weighted-average ordinary shares subject to forfeiture	(57)	(463)	(842)
Weighted-average ordinary shares used to compute basic and diluted net loss per share	69,461	62,345	55,610
Basic and diluted net loss per share	$ (2.87)	$ (4.46)	$ (4.25)

For the year ended December 31, 2021, 2020, and 2019, diluted and basic net loss per share were identical since potential ordinary shares were excluded from the calculation, as their effect was anti-dilutive.

Anti-dilutive Securities

The following ordinary equivalent shares were not included in the computation of diluted net loss per share because their effect was anti-dilutive:

	Year Ended December 31,		
(In thousands)	2021	2020	2019
Share issuances under equity incentive plans and ESPP	7,469	6,553	6,577
Share issuances upon the conversion of convertible senior notes	6,676	6,676	6,676
Total	14,145	13,229	13,253

In addition, there were 414,000 shares subject to performance-based vesting criteria which have been excluded from the ordinary equivalent shares table above for the year ended December 31, 2019. There were no such shares excluded as of December 31, 2021 and 2020.

Comprehensive Loss

Comprehensive loss is comprised of net loss and changes in unrealized gains and losses on the Company's available-for-sale investments.

Related Parties

GSK owned 13.0% of the Company's ordinary shares outstanding as of December 31, 2021. On June 22, 2020, GSK Finance (No.3) plc ("GSK Finance"), a wholly-owned subsidiary of GSK, issued $280,336,000 of exchangeable senior notes due 2023 (the "GSK Notes"), initially exchangeable into 9,644,792 ordinary shares of Theravance Biopharma held by GSK and its affiliates. The GSK Notes are guaranteed by GSK and are exchangeable at the option of noteholders on any business day on or after September 1, 2020. The GSK Notes will mature on June 22, 2023 and do not bear interest. The GSK Notes were offered at an issue price 108.5% of their principal amount. The initial exchange rate is 34.4044 shares of Theravance Biopharma ordinary shares per $1,000 principal amount of GSK Notes, which is equivalent to an initial exchange price of approximately $29.066 per share, representing a premium of 35% over the volume weighted-average price of Theravance Biopharma's ordinary shares on June 17, 2020.

Upon exchange of the GSK Notes, GSK Finance is expected to deliver its ordinary shares of Theravance Biopharma, but may at its option under certain circumstances, deliver cash or a combination of Theravance Biopharma ordinary shares and cash to noteholders. The GSK offering involves the expected exchange of substantially all of the 9,644,807 ordinary shares of Theravance Biopharma held by GSK and its affiliates. Theravance Biopharma will not be issuing any new ordinary shares in connection with the GSK offering, and Theravance Biopharma did not receive any proceeds from the GSK offering.

Robert V. Gunderson, Jr. was a member of the Company's board of directors until his resignation effective September 11, 2021. The Company has engaged Gunderson Dettmer Stough Villeneuve Franklin & Hachigian, LLP, of which Mr. Gunderson is a partner, as its primary legal counsel. Fees incurred for services provided by Gunderson Dettmer Stough Villeneuve Franklin & Hachigian, LLP were $0.5 million, $0.5 million and $0.4 million for the year ended December 31, 2021, 2020, and 2019, respectively.

Recently Adopted Accounting Pronouncements

In December 2019, the Financial Accounting Standards Board ("FASB") issued ASU 2019-12, *Income Taxes (Topic 740): Simplifying the Accounting for Income Taxes* ("ASU 2019-12") as part of its overall simplification initiative to reduce costs and complexity of applying accounting standards. ASU 2019-12 removes certain exceptions from Topic 740, *Income Taxes*, including (i) the exception to the incremental approach for intra period tax allocation when there is a loss from continuing operations and income or a gain from other items such as discontinued operations or other comprehensive income; (ii) the exception to accounting for outside basis differences of equity method investments and foreign subsidiaries; and (iii) the exception to limit the tax benefit recognized in interim periods in cases when the year-to-date losses exceed anticipated losses. ASU 2019-12 also simplifies GAAP in several other areas of Topic 740 such as

(i) franchise taxes and other taxes partially based on income; (ii) step-up in tax basis goodwill considered part of a business combination in which the book goodwill was originally recognized or should be considered a separate transaction; (iii) separate financial statements of entities not subject to tax; and (iv) interim recognition of enactment of tax laws or rate changes. ASU 2019-12 became effective for annual reporting periods and interim periods within those years beginning after December 15, 2020. The adoption of ASU 2019-12 did not have a material impact on the Company's consolidated financial statements and related disclosures.

Recently Issued Accounting Pronouncements Not Yet Adopted

In August 2020, the FASB issued ASU 2020-06, *Debt - Debt with Conversion and other Options (Subtopic 470-20) and Derivatives and Hedging: Contracts in Entity's Own Equity (Subtopic 815-40)* ("ASU 2020-06"). ASU 2020-06 simplifies the complexity associated with applying GAAP for certain financial instruments with characteristics of liabilities and equity by removing certain accounting models which separate the embedded conversion features from the host contract for convertible instruments. The standard also enhances the consistency of earnings-per-share calculations by requiring that an entity use the if-converted method and that the effect of potential share settlement be included in diluted earnings-per-share calculations. ASU 2020-06 is effective for fiscal years and interim periods within those fiscal years beginning after December 15, 2021. The Company evaluated ASU 2020-06 and determined that its adoption will not have a material impact on the Company's consolidated financial statements and related disclosures.

The Company has evaluated other recently issued accounting pronouncements and does not currently believe that any of these pronouncements will have a material impact on its consolidated financial statements and related disclosures.

2. Revenue

Revenues from Collaborative Arrangements

The Company recognized revenues from its collaborative arrangements as follows:

	Year Ended December 31,		
(In thousands)	**2021**	**2020**	**2019**
Janssen	$ 11,425	$ 26,426	$ 31,096
Other	38	38	154
Total collaboration revenue	$ 11,463	$ 26,464	$ 31,250

Changes in Deferred Revenue Balances

Changes in deferred revenue balances arose as a result of the Company recognizing the following revenue from collaborative arrangements during the periods below:

	Year Ended December 31,		
(In thousands)	**2021**	**2020**	**2019**
Collaboration revenue recognized in the period from:			
Amounts included in deferred revenue at the beginning of the period	$ 11,463	$ 26,464	$ 31,245
Performance obligations satisfied in previous period	—	—	—

Janssen Biotech

In February 2018, the Company entered into a global co-development and commercialization agreement with Janssen Biotech, Inc. ("Janssen") for izencitinib (formerly known as TD-1473) and related back-up compounds for inflammatory intestinal diseases, including ulcerative colitis and Crohn's disease (the "Janssen Agreement"). The Company received an upfront payment of $100.0 million.

Under the terms of the Janssen Agreement, following the initial Phase 2 development period, including the completion of the Phase 2 Crohn's study, Janssen had the right to obtain an exclusive license to develop and commercialize izencitinib and certain related back-up compounds by paying the Company $200.0 million. Upon any such election, the Company and Janssen would jointly develop and commercialize izencitinib in inflammatory intestinal diseases and share profits in the US and expenses related to Phase 3 development and registration activities (67% to

Janssen; 33% to Theravance Biopharma). The Company would receive royalties on ex-US sales at double-digit tiered percentage royalty rates, and the Company would be eligible to receive additional milestone payments from Janssen. In August 2021, the Company completed a Phase 2b/3 (RHEA) induction and maintenance study of izencitinib in ulcerative colitis and announced that the study results did not meet its primary endpoint. Based on the study results, in December 2021, the Company received notice from Janssen that the Janssen Agreement would be terminated effective January 16, 2022.

The Janssen Agreement was considered to be within the scope of Accounting Standards Codification, Topic 808, *Collaborative Arrangements* ("ASC 808") and the Company identified research and development activities as its performance obligations. The Company further determined that the transaction price under the arrangement was the $100.0 million upfront payment which was allocated to the performance obligations. The $200.0 million potential opt-in and other milestones payments were considered variable consideration and not included in the transaction price as they were all determined to be fully constrained under ASC 606. As part of the Company's evaluation of this variable consideration constraint, it determined that the potential payments are contingent upon developmental and regulatory milestones that are uncertain and are highly susceptible to factors outside of its control.

For the year ended December 31, 2021, 2020, and 2019, the Company recognized $11.4 million, $26.4 million, and $31.1 million, respectively, as revenue from collaboration arrangements related to the Janssen Agreement, and as of December 31, 2021, all of the revenue related to the $100.0 million upfront payment has been fully recognized as collaboration revenue.

Collaboration revenue was recognized for the research and development services based on a measure of the Company's efforts toward satisfying the performance obligation relative to the total expected efforts or inputs to satisfy the performance obligation (e.g., costs incurred compared to total budget). Consequently, delays in trial activity and/or changes to the total budget would have impacted the timing and amount of revenue recognized in any given reporting period. As a result of the notice from Janssen that the Janssen Agreement would be terminated effective January 16, 2022, the Company has no future performance obligations associated with the remaining collaboration revenue that was recognized in the fourth quarter of 2021. For the year ended December 31, 2021, 2020, and 2019, the Company incurred $18.3 million, $38.5 million, and $39.9 million, respectively, in research and development costs related to the Janssen Agreement.

Viatris

In January 2015, the Company and Viatris Inc. (formerly, Mylan Ireland Limited) ("Viatris") established a strategic collaboration (the "Viatris Agreement") for the development and commercialization of revefenacin, including YUPELRI® (revefenacin) inhalation solution. The Company entered into the collaboration to expand the breadth of its revefenacin development program and extend its commercial reach beyond the hospital setting.

As of December 31, 2021, the Company is eligible to receive from Viatris potential global (ex-China and adjacent territories) development, regulatory and sales milestone payments totaling up to $205.0 million in the aggregate, with $160.0 million associated with YUPELRI monotherapy, and $45.0 million associated with future potential combination products. Of the $160.0 million associated with monotherapy, $150.0 million relates to sales milestones based on achieving certain levels of net sales and $10.0 million relates to regulatory actions in the European Union ("EU"). The $45.0 million associated with future potential combination products relates solely to development and regulatory actions.

The Viatris Agreement is considered to be within the scope of ASC 808 and partially within the scope of ASC 606, as the parties are active participants and exposed to the risks and rewards of the collaborative activity with a unit of account provided to Viatris as a customer. Under the terms of the Viatris Agreement, which included the delivery by the Company of a license to Viatris to develop and commercialize revefenacin in exchange for $15.0 million received in 2015, Viatris was responsible for reimbursement of the Company's costs related to the registrational program up until the approval of the first new drug application in November 2018, thereafter, R&D expenses are shared. Performing R&D services for reimbursement is considered to be a collaborative activity under the scope of ASC 808. Reimbursable program costs are recognized proportionately with the performance of the underlying services and accounted for as reductions to R&D expense. For this unit of account, the Company did not recognize revenue or analogize to ASC 606

and, as such, the reimbursable program costs are excluded from the transaction price. The Company determined the license to develop and commercialize revefenacin to be a unit of account and a separate performance obligation for which Viatris is a customer with the $15.0 million for the delivery of the license as the transaction price.

The future potential milestone amounts for the Viatris Agreement were not included in the transaction price, as they were all determined to be fully constrained following the concepts of ASC 606. As part of the Company's evaluation of the development and regulatory milestones constraint, the Company determined that the achievement of such milestones is contingent upon success in future clinical trials and regulatory approvals which are not within its control and uncertain at this stage. The Company expects that the sales-based milestone payments and royalty arrangements will be recognized when the sales occur or the milestone is achieved.

The Company is also entitled to a share of US profits and losses (65% to Viatris; 35% to Theravance Biopharma) received in connection with commercialization of YUPELRI, and the Company is entitled to low double-digit tiered royalties on ex-US net sales. Viatris is the principal in the sales transactions, and as a result, the Company does not reflect the product sales in its consolidated financial statements.

Following the US Food and Drug Administration ("FDA") approval of YUPELRI in November 2018, net amounts payable to or receivable from Viatris each quarter under the profit-sharing structure are disaggregated according to their individual components. In accordance with the applicable accounting guidance, amounts receivable from Viatris in connection with the commercialization of YUPELRI are recorded within the consolidated statements of operations as revenue from "Viatris collaboration agreement" irrespective of whether the overall collaboration is profitable. Amounts payable to Viatris, if any, in connection with the commercialization of YUPELRI are recorded within the consolidated statements of operations as a collaboration loss within selling, general and administrative expenses. Any reimbursement from Viatris attributed to the 65% cost-sharing of the Company's R&D expenses is characterized as a reduction of R&D expense, as the Company does not consider performing research and development services for reimbursement to be a part of its ordinary activities.

The following YUPELRI-related amounts were recognized within revenue and selling, general and administrative expense in the Company's consolidated statements of operations:

	Year Ended December 31,		
(In thousands)	**2021**	**2020**	**2019**
Viatris collaboration agreement - *Amounts receivable from Viatris*	$ 43,848	$ 43,893	$ 13,664
Collaboration loss - *Amounts payable to Viatris*	$ —	$ —	$ 1,582

While Viatris records the total net sales of YUPELRI within its consolidated financial statements, Viatris collaboration agreement revenue includes the Company's implied 35% share of net sales of YUPELRI for the year ended December 31, 2021, 2020, and 2019 of $56.7 million, $50.0 million, and $19.3 million, respectively, before deducting shared expenses.

Reimbursement of R&D Expenses

As noted above, under certain collaborative arrangements the Company is entitled to reimbursement of certain R&D expenses. Activities under collaborative arrangements for which the Company is entitled to reimbursement are considered to be collaborative activities under the scope of ASC 808. For these units of account, the Company does not analogize to ASC 606 or recognize revenue. The Company records reimbursement payments received from its collaboration partners as reductions to R&D expense.

The following table summarizes the reductions to R&D expenses related to reimbursement payments:

(In thousands)	Year Ended December 31, 2021	2020	2019
Janssen	$ 5,819	$ 8,554	$ 5,129
Viatris	2,072	1,524	460
Total reduction to R&D expense, net	$ 7,891	$ 10,078	$ 5,589

Revenue from Licensing Arrangements

Viatris

In June 2019, the Company announced the expansion of the Viatris Agreement (the "Viatris Amendment") to grant Viatris exclusive development and commercialization rights to nebulized revefenacin in China and adjacent territories. In exchange, the Company received an upfront payment of $18.5 million (before a required tax withholding) and will be eligible to receive potential development and sales milestones totaling $54.0 million and low double-digit tiered royalties on net sales of nebulized revefenacin, if approved. Of the $54.0 million in potential milestones, $9.0 million is associated with the development of YUPELRI monotherapy, $7.5 million associated with the development of future potential combination products, and $37.5 million is associated with sales milestones. Viatris is responsible for all aspects of development and commercialization in the partnered regions, including pre- and post-launch activities and product registration and all associated costs.

The Viatris Amendment is accounted for under ASC 606 as a separate contract from the original Viatris Agreement that was entered into in January 2015. The Company identified a single performance obligation comprising of the delivery of the license to develop and commercialize revefenacin in China and adjacent territories. The transaction price was determined to be the upfront payment of $18.5 million which the Company recognized as licensing revenue following the completion of the performance obligation in June 2019.

The future potential milestone amounts for the Viatris Amendment were not included in the transaction price, as they were all determined to be fully constrained following the concepts of ASC 606. As part of the Company's evaluation of the development milestones constraint, the Company determined that the achievement of such milestones is contingent upon success in future clinical trials and regulatory approvals which are not within its control and uncertain at this stage. The Company expects that the sales-based milestone payments and royalty arrangements will be recognized when the sales occur or the milestone is achieved. The Company will re-evaluate the transaction price each quarter and as uncertain events are resolved or other changes in circumstances occur.

In March 2020, the Company earned a $1.5 million development milestone payment for the acceptance of a clinical trial application associated with the use of YUPELRI monotherapy in China and adjacent territories.

Pfizer

In December 2019, the Company entered into a global license agreement with Pfizer Inc. for its preclinical skin-selective, locally-acting pan-JAK inhibitor program (the "Pfizer Agreement"). The compounds in this program are designed to target validated pro-inflammatory pathways and are specifically designed to possess skin-selective activity with minimal systemic exposure.

Under the Pfizer Agreement, Pfizer has an exclusive license to develop, manufacture and commercialize certain compounds for all uses other than gastrointestinal, ophthalmic and respiratory applications. Under the terms of the Pfizer Agreement, the Company received an upfront cash payment of $10.0 million and is eligible to receive up to an additional $240.0 million in development and sales milestone payments from Pfizer. In addition, the Company will be eligible to receive a tiered royalty on worldwide net sales of any potential products under the license at percentage royalty rates ranging from middle single-digits to low double-digits.

The Pfizer Agreement is accounted for under ASC 606. The Company identified two performance obligations primarily comprised of the delivery of the license and samples of tangible materials which were completed in December 2019. The transaction price was determined to be the upfront payment of $10.0 million which the Company recognized as licensing revenue in December 2019.

The future potential milestones payable under the Pfizer Amendment were not included in the transaction price, as they were all determined to be fully constrained following the concepts of ASC 606. As part of the Company's evaluation of the development milestones constraint, the Company determined that the achievement of such milestones is contingent upon success in future clinical trials and regulatory approvals which are not within its control and uncertain at this stage. The Company expects that the sales-based milestone payments will be recognized when the sales occur or the milestone is achieved. The Company will re-evaluate the transaction price each quarter and as uncertain events are resolved or other changes in circumstances occur.

3. Segment Information

The Company operates in a single segment, which is the discovery (research), development and commercialization of human therapeutics. The following table summarizes total revenue by geographic region:

	Year Ended December 31,		
(In thousands)	**2021**	**2020**	**2019**
US	$ 55,273	$ 70,319	$ 54,760
Europe	38	1,538	18,654
Total revenue	$ 55,311	$ 71,857	$ 73,414

The following table summarizes total revenue from each of the Company's customers or collaboration partners who individually accounted for 10% or more of total revenue (as a percentage of total revenues) during the most recent three years:

	Year Ended December 31,		
(% of total revenue)	**2021**	**2020**	**2019**
Viatris	79 %	63 %	44 %
Janssen	21 %	37 %	42 %
Pfizer	—	—	14 %

4. Cash, Cash Equivalents, and Restricted Cash

The following table provides a reconciliation of cash, cash equivalents, and restricted cash reported within the current period and comparable prior year period consolidated balance sheets that sum to the total of the same such amounts shown on the consolidated statements of cash flows.

	December 31,		
(In thousands)	**2021**	**2020**	**2019**
Cash and cash equivalents	$ 89,959	$ 81,467	$ 58,064
Restricted cash	837	833	833
Total cash, cash equivalents, and restricted cash shown on the consolidated statements of cash flows	$ 90,796	$ 82,300	$ 58,897

The Company maintains restricted cash for certain lease agreements and letters of credit by which the Company has pledged cash and cash equivalents as collateral. The Company also maintains restricted cash for debt servicing of its 9.5% non-recourse 2035 notes. See *"Note 6. Debt"* for further information regarding the 9.5% non-recourse 2035 notes. The cash-related amounts reported in the table above exclude the Company's investments in short and long-term marketable securities that are reported separately on the consolidated balance sheets.

The Company periodically engages in foreign exchange transactions as a part of its operations. For the year ended December 31, 2021 and 2020, the Company recognized net realized and unrealized foreign currency losses of

$0.9 million and $0.3 million, respectively. For the year ended December 31, 2019, Company recognized net realized and unrealized foreign currency gains of $0.2 million. These amounts are included in the Company's consolidated statements of operations within "Interest and other income, net".

5. Investments and Fair Value Measurements

Available-for-Sale Securities

The estimated fair value of marketable securities is based on quoted market prices for these or similar investments obtained from a commercial pricing service. The fair market value of marketable securities classified within Level 1 is based on quoted prices for identical instruments in active markets. The fair value of marketable securities classified within Level 2 is based on quoted prices for similar instruments in active markets; quoted prices for identical or similar instruments in markets that are not active; or model-driven valuations whose inputs are observable or whose significant value drivers are observable. Observable inputs may include benchmark yields, reported trades, broker/dealer quotes, issuer spreads, two-sided markets, benchmark securities, bids, offers and reference data including market research publications.

Available-for-sale securities are summarized below:

		December 31, 2021			
(In thousands)		Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
US government securities	Level 1	$ 29,986	$ —	$ (2)	$ 29,984
Corporate notes	Level 2	5,034	—	(2)	5,032
Commercial paper	Level 2	48,490	1	(1)	48,490
Marketable securities		83,510	1	(5)	83,506
Money market funds	Level 1	50,228	—	—	50,228
Total		$ 133,738	$ 1	$ (5)	$ 133,734

		December 31, 2020			
(In thousands)		Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
US government securities	Level 1	$ 75,036	$ 34	$ —	$ 75,070
US government agency securities	Level 2	74,971	18	—	74,989
Corporate notes	Level 2	5,046	—	(1)	5,045
Commercial paper	Level 2	56,374	1	(5)	56,370
Marketable securities		211,427	53	(6)	211,474
Money market funds	Level 1	—	—	—	—
Total		$ 211,427	$ 53	$ (6)	$ 211,474

As of December 31, 2021, all of the Company's available-for-sale securities had contractual maturities within 6 months and the weighted-average maturity of marketable securities was approximately 2 months. There were no transfers between Level 1 and Level 2 during the periods presented, and there have been no material changes to the Company's valuation techniques during the year ended December 31, 2021 or 2020.

Available-for-sale debt securities with unrealized losses are summarized below:

	December 31, 2021					
	Less than 12 Months		Greater than 12 Months		Total	
(In thousands)	Estimated Fair Value	Gross Unrealized Losses	Estimated Fair Value	Gross Unrealized Losses	Estimated Fair Value	Gross Unrealized Losses
US government securities	$ 19,991	$ (2)	$ —	$ —	$ 19,991	$ (2)
Corporate notes	5,031	(2)	—	—	5,031	(2)
Commercial paper	9,995	(1)	—	—	9,995	(1)
Total	$ 35,017	$ (5)	$ —	$ —	$ 35,017	$ (5)

	December 31, 2020					
	Less than 12 Months		Greater than 12 Months		Total	
(In thousands)	Estimated Fair Value	Gross Unrealized Losses	Estimated Fair Value	Gross Unrealized Losses	Estimated Fair Value	Gross Unrealized Losses
Corporate notes	$ 5,045	$ (1)	$ —	$ —	$ 5,045	$ (1)
Commercial paper	39,375	(5)	—	—	39,375	(5)
Total	$ 44,420	$ (6)	$ —	$ —	$ 44,420	$ (6)

The Company invests primarily in high credit quality and short-term maturity debt securities with the intent to hold such securities until maturity at par value. The Company does not intend to sell the investments that are currently in an unrealized loss position, and it is unlikely that it will be required to sell the investments before recovery of their amortized cost basis, which may be at maturity. The Company reviewed its available-for-sale debt securities and determined that there were no credit-related losses to be recognized as of December 31, 2021.

As of December 31, 2021, the Company's accumulated other comprehensive income (loss) on its consolidated balance sheets included the net unrealized gains or losses on available-for-sale investments shown in the table above. For the year ended December 31, 2021, the Company did not sell any marketable securities. For the year ended December 31, 2020, the Company sold marketable securities for total proceeds of $19.9 million and recognized minimal net realized gains from the sales based on the specific identification method. The Company did not sell any of its marketable securities for the year ended December 31, 2019.

6. Debt

Debt consisted of the following liability components:

(In thousands)	December 31, 2021	2020
9.5% Non-Recourse 2035 Notes:		
Principal amount	$ 413,291	$ 418,572
Less: 5% retained by the Company	(20,665)	(20,929)
Unamortized debt issuance costs - 9.5% Non-Recourse 2035 Notes	(3,062)	(3,847)
Unamortized debt issuance costs - Modified 9.0% Non-Recourse 2033 Notes	(1,265)	(1,589)
	388,299	392,207
3.25% Convertible 2023 Notes:		
Principal amount	230,000	230,000
Unamortized debt issuance costs	(1,965)	(3,037)
	228,035	226,963
Total debt	$ 616,334	$ 619,170

Debt interest expense consists of the following components:

(In thousands)	Year Ended December 31, 2021	2020	2019
Stated coupon interest	$ 44,707	$ 42,625	$ 28,811
Amortization of debt issuance costs	2,182	1,960	3,051
Total debt interest expense	$ 46,889	$ 44,585	$ 31,862

9.5% Non-Recourse Notes Due 2035

On February 21, 2020, Theravance Biopharma R&D, Inc. (“Theravance R&D”), a wholly-owned subsidiary of the Company, and Triple Royalty Sub II LLC (the “Issuer II” or “Triple II”), a wholly-owned subsidiary of Theravance Biopharma R&D, entered into certain note purchase agreements (“Note Purchase Agreements”) with certain note purchasers (“Note Purchasers”), relating to the private placement by Issuer II of $400.0 million 9.5% Fixed Rate Term Notes due on or before 2035 (the “Non-Recourse 2035 Notes”). Ninety-five percent of the Non-Recourse 2035 Notes were sold to the Note Purchasers pursuant to the Note Purchase Agreements. The remaining 5% of the Non-Recourse 2035 Notes (the “Retained Notes”) were retained by the Company to comply with Regulation RR — Credit Risk Retention (17 C.F.R. Part 246). The Retained Notes are eliminated in the Company’s consolidated financial statements.

The Non-Recourse 2035 Notes are secured by all of Issuer II’s right, title and interest as a holder of certain membership interests (the “Issuer II Class C Units”) in TRC. TRC holds the right to receive upward-tiering royalties ranging from 6.5% to 10% on worldwide net sales of TRELEGY, and the Company holds an 85% economic interest in TRC. The Issuer II Class C Units represent 75% of the Company's 85% economic interest, which equates to 63.75% of the economic interests in TRC.

The source of principal and interest payments for the Non-Recourse 2035 Notes are the future royalty payments generated from the TRELEGY program, and as a result, the holders of the Non-Recourse 2035 Notes have no recourse against the Company even if the TRELEGY payments are insufficient to cover the principal and interest payments for the Non-Recourse 2035 Notes. Prior to and including the December 5, 2024 payment date, in the event that the distributions received by the Issuer II from TRC in a quarter are less than the interest accrued for that quarter, the principal amount of the Non-Recourse 2035 Notes will increase by the interest shortfall amount for that quarter. While the holders of the Non-Recourse 2035 Notes have no recourse against the Company, the terms of the Non-Recourse 2035 Notes also provide that the Company, at its option, may satisfy the quarterly interest payment obligations by making a capital contribution to the Issuer II.

Over the course of 2021, $5.7 million of net interest shortfall was added to and $10.7 million of net principal payments was deducted from the Non-Recourse 2035 Notes. This resulted in a $5.0 million net principal decrease of the Non-Recourse 2035 Notes which represented royalties received in excess of the interest payable through the respective payment dates. As of December 31, 2021, the Non-Recourse 2035 Notes' issuance-to-date net interest shortfall was $23.4 million and the issuance-to-date net principal paydown was $10.7 million.

The Non-Recourse 2035 Notes are not convertible into Company equity and have no security interest in nor rights under any agreement with GSK. The Non-Recourse 2035 Notes may be redeemed by Issuer II on and after February 28, 2022, in whole or in part, at specified redemption premiums. The Non-Recourse 2035 Notes bear an annual interest rate of 9.5%, with interest and principal paid quarterly beginning June 5, 2020. Since the principal and interest payments on the Non-Recourse 2035 Notes are ultimately based on royalties from TRELEGY product sales, which will vary from quarter to quarter, the Non-Recourse 2035 Notes may be repaid prior to the final maturity date in 2035. Following the redemption or repayment of the Non-Recourse 2035 Notes, all TRELEGY-related pledged cash flows will revert to the Company.

As of December 31, 2021, the net principal and estimated fair value of the Non-Recourse 2035 Notes were $392.6 million and $373.0 million, respectively. As of December 31, 2020, the net principal and estimated fair value of the Non-Recourse 2035 Notes were $397.6 million and $399.6 million, respectively. The inputs to determine fair value of the Non-Recourse 2035 Notes are categorized as Level 2 inputs. Level 2 inputs include quoted prices for similar instruments in active markets; quoted prices for identical or similar instruments in markets that are not active; and model-derived valuations whose inputs are observable or whose significant value drivers are observable.

9.0% Non-Recourse Notes Due 2033

In November 2018, the Company entered into note purchase agreements relating to the private placement of $250.0 million aggregate principal amount of 9.0% non-recourse notes, due on or before 2033 (the "Non-Recourse 2033 Notes") issued by the Company's wholly-owned subsidiary, Triple Royalty Sub LLC (the "Issuer"). On February 28, 2020, the Company refinanced the Non-Recourse 2033 Notes by issuing the Non-Recourse 2035 Notes and a portion of those proceeds were used to repay, in full, the remaining outstanding balance of the Company's Non-Recourse 2033 Notes. Pursuant to the terms of the Non-Recourse 2033 Notes, the Company paid a debt redemption premium of 5% of the outstanding principal as of the refinancing date.

The refinancing of the Non-Recourse 2033 Notes involved multiple lenders who were considered members of a loan syndicate. To determine whether the refinancing was to be accounted for as a debt extinguishment or modification, the Company considered whether the lenders involved in the Non-Recourse 2033 Notes and the Non-Recourse 2035 Notes remained the same or changed and whether the change in debt terms was substantial. The debt terms were considered substantially different if the present value of the cash inflows and outflows of the Non-Recourse 2035 Notes, including all principal increases and lender fees on the refinancing date, was at least 10% different from the present value of the remaining cash inflows and outflows of the Non-Recourse 2033 Notes (the "10% Test"). The Company performed the 10% Test for each individual lender participating in the loan syndication by assuming the exercise and non-exercise of the prepayment option. The cash flow assumption generating the smaller change was used as the basis for determining whether the 10% threshold was met. For existing lenders who participated in the Non-Recourse 2035 Notes as part of the new loan syndicate, the refinancing was accounted for as an extinguishment or a modification depending upon whether the change in the cash flows was more or less than 10%, respectively. Amounts due to lenders of the Non-Recourse 2033 Note offering who did not participate in the Non-Recourse 2035 Notes were accounted for as a debt extinguishment.

For debt determined to be extinguished, the total unamortized deferred financing costs and the associated redemption premium of $15.5 million were expensed as "Loss on extinguishment of debt" within the consolidated statements of operations for the year ended December 31, 2020. In addition, $0.3 million of new third-party costs were expensed, and $4.4 million of new creditor fees were capitalized as debt discount. For debt determined to be modified, $0.5 million of new creditor fees were expensed, and the related unamortized deferred financing costs of $1.8 million, as of February 28, 2020, will continue to be amortized through the remaining term of the Non-Recourse 2035 Notes.

3.25% Convertible Senior Notes Due 2023

In November 2016, the Company completed an underwritten public offering of $230.0 million of 3.25% convertible senior notes, due 2023 (the "Convertible Senior 2023 Notes") for net proceeds of $222.5 million. The Company incurred $7.5 million in debt issuance costs, which are being amortized to interest expense over the estimated life of the Convertible Senior 2023 Notes. The Convertible Senior 2023 Notes bear an annual interest rate of 3.25%, payable semi-annually in arrears, on November 1 and May 1 of each year.

The Convertible Senior 2023 Notes are senior unsecured obligations and rank senior in right of payment to any of the Company's indebtedness that is expressly subordinated in right of payment to the Convertible Senior 2023 Notes; equal in right of payment to any of the Company's indebtedness that is not so subordinated; effectively junior in right of payment to any of the Company's secured indebtedness to the extent of the value of the assets securing such indebtedness; and structurally junior to all indebtedness and other liabilities (including trade payables) of the Company's subsidiaries.

The Convertible Senior 2023 Notes will mature on November 1, 2023, unless earlier redeemed or repurchased by the Company or converted. Holders may convert their Convertible Senior 2023 Notes into ordinary shares at an initial conversion rate of 29.0276 shares for each $1,000 principal amount of Convertible Senior 2023 Notes, which is equivalent to an initial conversion price of approximately $34.45 per share, subject to adjustment, in certain circumstances (including upon the occurrence of a fundamental change), at any time prior to the close of business on the second business day immediately preceding the maturity date. Upon the occurrence of a fundamental change involving the Company, holders of the Convertible Senior 2023 Notes may require the Company to repurchase all or a portion of their Convertible Senior 2023 Notes for cash at a redemption price equal to 100% of the principal amount of the Convertible Senior 2023 Notes to be redeemed, plus accrued and unpaid interest to, but excluding, the fundamental change repurchase date. In addition, in some circumstances, the conversion rate of the Convertible Senior 2023 Notes will increase with a make whole premium for conversions in connection with certain fundamental changes.

The debt issuance costs related to the Convertible Senior 2023 Notes offering were capitalized as deferred financing costs and presented as a reduction of the carrying value of the financial liability on the Company's consolidated balance sheets at December 31, 2021 and 2020.

The estimated fair value of the Convertible Senior 2023 Notes was $220.2 million and $217.9 million at December 31, 2021 and 2020, respectively. The estimated fair value was primarily based upon the underlying price of Theravance Biopharma's publicly traded shares and other observable inputs as of December 31, 2021 and 2020. The inputs to determine fair value of the Convertible Senior 2023 Notes are categorized as Level 2 inputs. Level 2 inputs include quoted prices for similar instruments in active markets; quoted prices for identical or similar instruments in markets that are not active; and model-derived valuations whose inputs are observable or whose significant value drivers are observable.

7. Leases

As of December 31, 2021, the Company leased approximately 162,000 square feet of office and laboratory space in two buildings in South San Francisco, California, under a non-cancelable operating lease that ends in May 2030 ("SSF Lease"). The lease includes a tenant improvement allowance that expires in November 2022 and had a remaining balance of $10.2 million and $12.1 million, as of December 31, 2021 and 2020, respectively. The Company's Irish subsidiary leases approximately 6,100 square feet of office space in Dublin, Ireland under a lease that expires in April 2027 ("Dublin Lease").

In July 2021, the Company terminated approximately 8,000 square feet of original office space in one of the buildings and returned the space to the building's landlord for their use. The Company determined that the termination would be accounted for as a lease modification under ASC 842, *Leases* ("ASC 842"). As a result of the modification, the Company reduced the value of its operating lease assets and liabilities in the consolidated balance sheets, by $1.1 million and $3.0 million, respectively, resulting in a gain of $1.9 million which partially offset operating expenses in the consolidated statements of operations.

Additionally, in July 2021, the Company entered into a separate agreement under which it subleased approximately 21,000 square feet of its South San Francisco office and laboratory space, effective October 2021. Under the terms of the sublease agreement, the sublease term continues through September 2028, and the parties have no option to extend the sublease. Either the Company or the subtenant may terminate the sublease by giving the other party ten days prior written notice. The Company is entitled to receive an initial monthly base rent of $0.1 million, with annual base rent increases of 3% and the subtenant's proportionate share of the building's operating expenses. The Company expects to receive a total of $13.1 million over the sublease term which represents a $3.8 million premium over its proportionate lease payment obligations under the head lease. Under the terms of the head lease, 50% of the sublease premium, equal to $1.9 million, shall be shared with the landlord and 50% shall be retained by the Company. In October 2021, the Company began recognizing the sublease income on a straight-line basis over the term of the sublease which was reflected as a reduction in operating expenses in the consolidated statements of operations. No lease modification was deemed to have occurred by entering into the sublease agreement because the Company was not released, either fully or in part, from its obligations under the head lease with the landlord.

The SSF Lease contains two options to extend the term of the lease for successive periods of five years each, and the Dublin Lease contains a lease termination option in April 2024 at the Company's discretion. The two options to extend the SSF Lease and the option to terminate the Dublin Lease were not recognized in the determination of the Company's right-of-use assets and lease liabilities below.

The Company has evaluated its leases and determined that they were all operating leases. The present values of the remaining lease payments and corresponding right-of-use assets were as follows, and the difference between the right-of-use assets and lease liabilities was primarily due to office-related deferred rent payments that are payable in future periods and tenant improvement reimbursements.

(In thousands)	Classification	December 31, 2021	December 31, 2020
Assets			
Operating lease assets	Operating lease assets	$ 39,690	$ 43,260
Liabilities			
Current:			
Operating lease liabilities	Operating lease liabilities	$ 503	$ 9,867
Non-current:			
Operating lease liabilities	Long-term operating lease liabilities	52,681	47,220
Total operating lease liabilities		$ 53,184	$ 57,087

Lease expense and sublease income were included within operating expenses in the consolidated statements of operations as follows:

(In thousands)	Classification	Year Ended December 31, 2021	Year Ended December 31, 2020	Year Ended December 31, 2019
Operating lease expense	Selling, general and administrative expense	$ 6,248	$ 7,974	$ 7,959
Operating lease expense	Research and development expense	1,377	758	164
Total operating lease expense [1]		$ 7,625	$ 8,732	$ 8,123

(In thousands)	Classification	Year Ended December 31, 2021	Year Ended December 31, 2020	Year Ended December 31, 2019
Operating sublease income	Selling, general and administrative expense	$ 466	$ —	$ —

(1) Excludes short-term leases which were not material and office lease service-related charges.

Cash paid for amounts included in the measurement of lease liabilities was as follows:

(In thousands)	Year Ended December 31, 2021	Year Ended December 31, 2020
Cash paid for amounts included in the measurement of lease liabilities:		
Operating cash flows from operating leases	$ 8,971	$ 3,804

As of December 31, 2021, the maturities of the Company's lease liabilities were as follows:

(In thousands)	
Year ending December 31:	
2022	$ 9,390
2023	9,655
2024	9,865
2025	10,133
2026	10,425
Thereafter	36,552
Total operating lease payments	$ 86,020
Less: Estimated tenant improvement allowance	(10,214)
Less: Imputed interest	(22,622)
Present value of operating lease liabilities	$ 53,184

As of December 31, 2021, the undiscounted cash flows to be received related to the Company's sublease were as follows:

(In thousands)	
Year ending December 31:	
2022	$ 1,717
2023	1,768
2024	1,821
2025	1,876
2026	1,932
Thereafter	3,516
Total operating sublease receipts	$ 12,630

As of December 31, 2021, the weighted-average remaining lease term was 8.3 years, and the weighted-average discount rate used to determine the lease liabilities was 8.64%. The Company's discount rate was primarily derived from the 9.0% interest rate on its previously issued Non-Recourse 2033 Notes in November 2018 and did not involve any significant assumptions.

8. Theravance Respiratory Company, LLC

Through the Company's 85% equity interest in TRC, the Company is entitled to receive an 85% economic interest in any future payments made by GSK under the strategic alliance agreement and under the portion of the collaboration agreement assigned to TRC (net of TRC expenses paid and the amount of cash, if any, expected to be used by TRC pursuant to the TRC LLC Agreement over the next four fiscal quarters). The primary drug program assigned to TRC is TRELEGY.

In May 2014, the Company entered into the TRC LLC Agreement with Innoviva, Inc. ("Innoviva") that governs the operation of TRC. Under the TRC LLC Agreement, Innoviva is the manager of TRC, and the business and affairs of TRC are managed exclusively by the manager, including (i) day to day management of the drug programs in accordance with the existing GSK agreements; (ii) preparing an annual operating plan for TRC; and (iii) taking all actions necessary to ensure that the formation, structure and operation of TRC complies with applicable law and partner agreements. The

Company is responsible for its proportionate share of TRC's administrative expenses incurred, and communicated to the Company, by Innoviva.

The Company analyzed its ownership, contractual and other interests in TRC to determine if it is a variable-interest entity ("VIE"), whether the Company has a variable interest in TRC and the nature and extent of that interest. The Company determined that TRC is a VIE. The party with the controlling financial interest, the primary beneficiary, is required to consolidate the entity determined to be a VIE. Therefore, the Company also assessed whether it is the primary beneficiary of TRC based on the power to direct TRC's activities that most significantly impact TRC's economic performance and its obligation to absorb TRC's losses or the right to receive benefits from TRC that could potentially be significant to TRC. Based on the Company's assessment, the Company determined that it is not the primary beneficiary of TRC, and, as a result, the Company does not consolidate TRC in its consolidated financial statements. TRC is recognized in the Company's consolidated financial statements under the equity method of accounting.

For the year ended December 31, 2021, 2020, and 2019, the Company recognized net royalty income of $104.0 million, $68.4 million, and $33.7 million, respectively, in the consolidated statements of operations within "Income from investment in TRC, LLC". These amounts were recorded net of the Company's share of TRC's expenses of $3.4 million, $2.2 million, $2.7 million for the year ended December 31, 2021, 2020, and 2019, respectively. The Company's share of TRC expenses for 2021, 2020, and 2019 was primarily comprised of TRC legal and related fees associated with the arbitration between Innoviva, as the manager of TRC, and TRC and the Company (*see below for more information regarding the arbitration*).

For the year ended December 31, 2021, the Company received $59.5 million from TRC related to TRELEGY royalties, and as of December 31, 2021, the amounts due from TRC of $43.5 million were recorded as a current asset in the consolidated balance sheets within "Amounts due from TRC, LLC". The Company has also recorded $67.5 million as a long-term asset within "Equity in net assets of TRC, LLC" in the consolidated balance sheets which represented its share of TRC's net assets which included funds withheld by TRC for future investments. For the year ended December 31, 2021, the Company recognized a net unrealized loss of $0.3 million associated with the estimated fair market value of certain equity investments previously made by TRC.

TRC's summary financial information, including the portion of equity interest that the Company does not own, was as follows as of or for the year ended December 31:

	Year Ended December 31,		
(In thousands)	**2021**	**2020**	**2019**
Current assets	$ 93,275	$ 63,027	$ 36,737
Non-current assets	37,695	16,959	—
Current liabilities	252	508	3,069
Royalty revenue and gross profit	126,688	73,089	42,790
Revenue from collaborative arrangements for the period ended	—	10,000	—
Income from continuing operations	122,732	80,477	39,410
Net income	$ 121,191	$ 81,662	$ 39,653

SEC Rule 3-09 of Regulation S-X requires that a company include audited financial statements for equity method investees when such investees are individually significant for a company's fiscal year. For the year ended December 31, 2021, the income from the Company's investment in TRC was determined to be significant. As a result, TRC's audited financial statements for the year ended December 31, 2021 were included as Exhibit 10.72 in this Annual Report on Form 10-K.

TRC Arbitration

The Company initiated an arbitration proceeding in October 2020 against Innoviva and TRC, challenging the authority of Innoviva and TRC to pursue a business plan to use TRELEGY royalties to invest in certain privately-held companies, rather than distribute such funds that would otherwise be available for distribution to the Company under the

terms of the TRC LLC Agreement to the Company in a manner that it believes is consistent with the TRC LLC Agreement and its 85% economic interest in TRC.

On March 30, 2021, the arbitrator ruled that, the Company had not shown that at the then current levels of investment, Innoviva and TRC had not breached the TRC LLC Agreement as of the date of the arbitration. The arbitrator further ruled that Innoviva and TRC had not breached the implied covenant of good faith and fair dealing; or their fiduciary duties. The arbitrator also ruled that (i) Innoviva is entitled to indemnification from TRC for all legal fees and expenses reasonably incurred in the arbitration and (ii) the Company is entitled to indemnification from TRC for legal fees and costs incurred in defending an action Innoviva brought against it in the Delaware Court of Chancery. The arbitrator noted in the ruling that although the Company failed to show that Innoviva's investment activities, at the then current levels of investment, have or will have a material and adverse effect on its economic interest in TRC, this does not mean that any future investments or actions will not require the Company's consent. The arbitrator noted in the ruling that the Company may, in the future, have a consent right over the decision to continue this investment strategy or whether to make a particular investment if, for example, Innoviva develops a track record of poor investments, over allocates royalties to these investment activities, or fails to distribute sufficient investment returns, and such facts cause the strategy or investment to have a material adverse effect on the Company's economic interest in TRC.

Pursuant to the terms of the TRC LLC Agreement, Innoviva is required to deliver to the Company a draft quarterly financial plan 30 days prior to the end of each fiscal quarter covering the next fiscal quarter. While the TRC LLC Agreement provides that Innoviva must consider in good faith any comments the Company provides, an applicable financial plan becomes effective 30 days after the draft plan is provided to the Company. The Company has objected to the proposed investments in private companies presented in draft TRC quarterly financial plans to date. If TRC identifies and consummates investments and incurs associated fees identified in a TRC quarterly plan, even over the Company's objections, distributions by TRC to its members in subsequent quarters will be reduced.

The Company's objections with regard to a TRC quarterly plan or other actions by TRC could result in additional legal proceedings between the Company, TRC and Innoviva, as was the case when the Company initiated arbitration proceedings against Innoviva and TRC in May 2019 and again in October 2020. Any such legal proceedings could divert the attention of management and cause the Company to incur significant costs, regardless of the outcome, which the Company cannot predict. If such proceedings were pursued, there can be no assurance that they would result in the Company receiving additional distributions from TRC. An adverse result could materially and adversely affect the funds that the Company would otherwise expect to receive from TRC in the future.

9. Property and Equipment

Property and equipment are held predominantly in the US and consisted of the following:

	December 31,	
(In thousands)	**2021**	**2020**
Computer equipment	$ 2,341	$ 2,314
Software	2,063	2,076
Furniture and fixtures	3,605	3,812
Laboratory equipment	20,087	29,753
Leasehold improvements	24,053	24,275
Subtotal	52,149	62,230
Less: accumulated depreciation	(38,492)	(45,808)
Property and equipment, net	$ 13,657	$ 16,422

For the year ended December 31, 2021, 2020, and 2019, depreciation expense for property and equipment was $3.5 million, $3.3 million, and $3.3 million, respectively.

As a result of the Company's corporate restructuring announcement in September 2021 (see *"Note 14. Corporate Restructuring"*), the Company completed an auction of certain property and equipment in December 2021. In January 2022, the Company received net proceeds of $1.9 million from the auction, and the net realized loss from the sale of the property and equipment was not material.

10. Share-Based Compensation

Theravance Biopharma Equity Plans

The Company has three equity compensation plans — its 2013 Equity Incentive Plan (the "2013 EIP"), its 2013 Employee Share Purchase Plan (the "2013 ESPP") and its 2014 New Employee Equity Incentive Plan (the "2014 NEEIP"). At inception, the Company was authorized to issue 5,428,571 ordinary shares under the 2013 EIP, 857,142 ordinary shares under the 2013 ESPP, and 750,000 ordinary shares under the 2014 NEEIP.

The 2013 EIP provides for the issuance of share-based awards, including restricted shares, restricted share units, options, share appreciation rights ("SARs") and other equity-based awards, to Company employees, officers, directors and consultants. As of January 1 of each year, commencing on January 1, 2015 and ending on (and including) January 1, 2023, the aggregate number of ordinary shares that may be issued under the 2013 EIP shall automatically increase by a number equal to the least of 5% of the total number of ordinary shares outstanding on December 31 of the prior year, 3,428,571 ordinary shares, or a number of ordinary shares determined by the Company's board of directors. Options may be granted with an exercise price not less than the fair market value of the ordinary shares on the grant date. Under the terms of the Company's 2013 EIP, options granted to employees generally have a maximum term of 10 years and vest over a four-year period from the date of grant; 25% vest at the end of one year, and 75% vest monthly over the remaining three years. The Company may grant options with different vesting terms from time to time. Unless an employee's termination of service is due to disability or death, upon termination of service, any unexercised vested options will generally be forfeited at the end of three months or the expiration of the option, whichever is earlier.

Under the 2013 ESPP, the Company's officers and employees may purchase ordinary shares through payroll deductions at a price equal to 85% of the lower of the fair market value of the ordinary share at the beginning of the offering period or at the end of each applicable purchase period. As of January 1 of each year, commencing on January 1, 2015 and ending on (and including) January 1, 2033, the aggregate number of ordinary shares that may be issued under the 2013 ESPP shall automatically increase by a number equal to the least of 1% of the total number of ordinary shares outstanding on December 31 of the prior year, 571,428 ordinary shares or a number of ordinary shares determined by the Company's board of directors. The ESPP generally provides for consecutive and overlapping offering periods of 24 months in duration, with each offering period generally composed of four consecutive six-month purchase periods. The purchase periods end on either May 15 or November 15. ESPP contributions are limited to a maximum of 15% of an employee's eligible compensation. The 2013 ESPP also includes a feature that provides for the existing offering period to terminate and for participants in that offering period to automatically be enrolled in a new offering period when the fair market value of an ordinary share at the beginning of a subsequent offering period falls below the fair market value of an ordinary share on the first day of such offering period.

The 2014 NEEIP provides for the issuance of share-based awards, including restricted shares, restricted share units, non-qualified options and SARs, to the Company's employees. Options may be granted with an exercise price not less than the fair market value of the ordinary shares on the grant date. Under the terms of the 2014 NEEIP, options granted to employees generally have a maximum term of 10 years and vest over a four-year period from the date of grant; 25% vest at the end of one year, and 75% vest monthly over the remaining three years. The Company may grant options with different vesting terms from time to time. Unless an employee's termination of service is due to disability or death, upon termination of service, any unexercised vested options will generally be forfeited at the end of three months or the expiration of the option, whichever is earlier.

Performance-Contingent Awards

In 2016, the Compensation Committee of the Company's board of directors ("Compensation Committee") approved the grant of 1,575,000 performance-contingent restricted share awards ("RSAs") and 135,000 performance-contingent restricted share units ("RSUs") to senior management. The vesting of such awards was dependent on the Company meeting its critical operating goals and objectives during the five-year period from 2016 to December 2020, as well as, continued employment. The awards were broken into three separate tranches, and expenses associated with these awards were recognized during the years 2016 to 2020 as the performance conditions were achieved. As of the first quarter of 2020, the performance conditions associated with all three tranches were achieved. The Company recognized $0.4 million, $3.0 million, and $1.9 million of share-based compensation expense associated with these awards for the

year ended December 31, 2021, 2020, and 2019, respectively, and the expenses associated with these awards have been fully recognized as of December 31, 2021.

Separate from the performance-contingent awards described above, the Company periodically grants performance-contingent RSUs to employees. For the year ended December 31, 2021, 2020, and 2019, the Company recognized $0.4 million, $1.0 million, and $1.0 million, respectively, of share-based compensation expense related to such awards. As of December 31, 2021, there were 325,000 shares of these performance-contingent RSUs outstanding that have a maximum remaining share-based compensation expense of $2.9 million with performance expiration dates through December 2025.

Share-Based Compensation Modifications Due to Corporate Restructuring

As a result of the Company's corporate restructuring announcement in September 2021 (see *"Note 14. Corporate Restructuring"*), the Board of Directors' Compensation Committee approved the acceleration of certain equity awards for employees affected by the restructuring. The Company accounted for this acceleration as a Type III modification (improbable to probable) which resulted in a fair value of $5.6 million as of the modification date, which was recorded in "Restructuring and related expenses" within the consolidated statements of operations. The total cumulative compensation cost previously recognized for these awards of $2.8 million within "Research and development" and "Selling, general and administrative" through the modification date, was reversed. The acceleration resulted in a net incremental share-based compensation expense of $2.8 million for the year ended December 31, 2021 and impacted approximately 160 terminated employees that met the conditions of the acceleration.

Share-Based Compensation Expense

Share-based compensation expense included in the consolidated statements of operations was recognized as follows:

	Year Ended December 31,		
(In thousands)	**2021**	**2020**	**2019**
Research and development	$ 25,634	$ 31,294	$ 28,953
Selling, general and administrative	28,065	31,682	31,497
Restructuring and related expenses	8,362	—	—
Total share-based compensation expense	$ 62,061	$ 62,976	$ 60,450

Share-based compensation expense included in the consolidated statements of operations by award type was as follows:

	Year Ended December 31,		
(In thousands)	**2021**	**2020**	**2019**
Innoviva equity:			
Options	$ —	$ —	$ —
RSUs	—	—	—
RSAs	—	—	64
Performance RSAs	—	—	—
Theravance Biopharma equity:			
Options	5,473	6,536	6,381
RSUs	54,931	49,803	39,520
Performance RSAs and RSUs	763	3,943	12,717
ESPP	894	2,694	1,768
Total share-based compensation expense	$ 62,061	$ 62,976	$ 60,450

As of December 31, 2021, the unrecognized share-based compensation cost, net of actual forfeitures, and the estimated weighted-average amortization period, using the straight-line attribution method, was as follows:

(In thousands, except amortization period)	Unrecognized Compensation Cost	Weighted-Average Amortization Period (Years)
Theravance Biopharma equity:		
Options	$ 4,535	1.98
RSUs	88,220	2.77
Performance RSAs and RSUs [1]	795	2.37
ESPP	1	0.70
Total	$ 93,551	

(1) Represents unrecognized share-based compensation cost associated with the Company's performance-contingent awards described above that are probable of vesting.

Compensation Awards

The following table summarizes option activity under the 2013 EIP and 2014 NEEIP for the year ended December 31, 2021:

	Number of Shares Subject to Outstanding Options	Weighted-Average Remaining Contractual Term (Years)	Exercise Price of Outstanding Options (in dollars)	Aggregate Intrinsic Value (in thousands)
Outstanding at December 31, 2020	3,299,179		$ 24.58	
Granted	230,750		18.85	
Exercised	(275)		16.76	
Forfeited	(658,086)		22.41	
Outstanding at December 31, 2021	2,871,568	4.63	24.62	$ 1,070
Exercisable at December 31, 2021		3.95		867
Vested and expected to vest at December 31, 2021		4.62		1,070

The following table summarizes additional information for options under the 2013 EIP and 2014 NEEIP.

	2021	2020	2019
Weighted average fair value of options (in dollars)	$ 9.25	$ 11.03	$ 10.20
Total intrinsic value of options exercised (in thousands)	$ 1	$ 384	$ 822

The following table summarizes total RSU and RSA activity (including performance RSUs and RSAs) for the year ended December 31, 2021:

	Number of Shares Subject to Outstanding RSUs	Number of Shares Outstanding Subject to Performance Conditions (RSAs)
Outstanding at December 31, 2020	4,993,918	414,000
Granted	7,850,175	—
Released	(2,682,186)	(414,000)
Forfeited	(1,808,058)	—
Outstanding at December 31, 2021	8,353,849	—

The total estimated fair value of RSUs vested was $49.3 million and $52.8 million in 2021 and 2020, respectively.

Valuation Assumptions

The range of assumptions used to estimate the fair value of options granted and rights granted under the 2013 ESPP was as follows:

	Year Ended December 31,		
	2021	2020	2019
Options			
Risk-free interest rate	0.5% - 1.2%	0.3% - 1.7%	1.6% - 2.5%
Expected term (in years)	5.3 - 6.1	5.2 - 6.1	6.0
Volatility	52% - 53%	50% - 53%	51% - 53%
Dividend yield	—	—	—
Weighted-average estimated fair value	$ 9.25	$ 11.03	$ 10.20
2013 ESPP			
Risk-free interest rate	0.03% - 0.2%	0.1% - 0.2%	1.5% - 2.4%
Expected term (in years)	0.5 - 2.0	0.5 - 2.0	0.5 - 2.0
Volatility	40% - 79%	53% - 76%	40% - 48%
Dividend yield	—	—	—
Weighted-average estimated fair value	$ 3.52	$ 8.04	$ 6.17

11. Income Taxes

Theravance Biopharma was incorporated in the Cayman Islands in July 2013 under the name Theravance Biopharma, Inc. as a wholly-owned subsidiary of Innoviva and began operations subsequent to a spin-off with wholly-owned subsidiaries in the Cayman Islands, US, United Kingdom, and Ireland. Effective July 1, 2015, Theravance Biopharma became an Irish tax resident, therefore, the loss before income taxes of Theravance Biopharma, the parent company, are included in Ireland in the tables below.

The components of the loss before income taxes were as follows:

	Year Ended December 31,		
(In thousands)	2021	2020	2019
Income (loss) before provision for income taxes:			
Cayman Islands	$ —	$ 37,567	$ 11,779
United States	(16,568)	(46,500)	(99,225)
Ireland	(182,775)	(277,105)	(154,217)
United Kingdom	(234)	(499)	(14)
Total	$ (199,577)	$ (286,537)	$ (241,677)

The components of provision for income tax benefit were as follows:

	Year Ended December 31,		
(In thousands)	2021	2020	2019
Provision for income tax benefit (expense):			
Current:			
Cayman Islands	$ —	$ —	$ —
United States	173	8,545	5,210
Ireland	(8)	(13)	—
United Kingdom	(14)	(12)	12
Subtotal	151	8,520	5,222
Deferred	—	—	—
Total	$ 151	$ 8,520	$ 5,222
Effective tax rate	0.08 %	2.97 %	2.16 %

The provision for income tax benefit was $0.2 million, $8.5 million, and $5.2 million for the year ended December 31, 2021, 2020, and 2019, respectively.

The 2021 and 2020 net income tax benefit was primarily attributed to a reversal of previously accrued contingent tax liabilities for uncertain tax positions due to a lapse of the statute of limitations and their related interest accruals. The 2019 net income tax benefit was primarily due to the reversal of previously accrued contingent tax liabilities for uncertain tax positions due to a lapse of the statute of limitations and current year US research and development credits.

No provision for income taxes has been recognized on undistributed earnings of the Company's foreign subsidiaries because it considers such earnings to be indefinitely reinvested. In the event of a distribution of these earnings in the form of dividends or otherwise, the Company may be liable for income taxes, subject to an adjustment, if any, for foreign tax credits and foreign withholdings taxes payable to certain foreign tax authorities. As of December 31, 2021, there were no undistributed earnings.

As a result of the Company becoming an Irish tax resident effective July 1, 2015, the tax rates reflect the Irish statutory rate of 25%. The differences between the Irish statutory income tax rate and the Company's effective tax rates were as follows:

	Year Ended December 31,		
	2021	2020	2019
Provision at statutory income tax rate	25.00 %	25.00 %	25.00 %
Foreign rate differential	(10.52)	(11.49)	(6.96)
Share-based compensation	(4.14)	0.75	(1.17)
Non-deductible executive compensation	(1.62)	(0.63)	(0.51)
Uncertain tax positions	(5.25)	(1.26)	(0.63)
Research and development tax credit carryforwards	2.38	1.83	2.50
Intangible asset	2.44	10.01	—
Change in valuation allowance	(7.62)	(20.56)	(14.90)
Other	(0.59)	(0.68)	(1.17)
Effective tax rate	0.08 %	2.97 %	2.16 %

Deferred income taxes reflect the net tax effects of temporary differences between the carrying amounts of assets and liabilities for financial reporting purposes and the amounts used for income tax purposes. Significant components of the Company's deferred tax assets and liabilities were as follows:

(In thousands)	December 31, 2021	2020
Deferred tax assets:		
Net operating loss carryforwards	$ 115,606	$ 82,821
Capital loss carryforwards	19,409	19,409
Research and development tax credit carryforwards	28,372	24,075
Fixed assets and intangibles	287,177	310,187
Share-based compensation	10,432	15,087
Accruals	3,590	8,145
Operating lease liabilities	11,607	11,662
Other	10,505	346
Subtotal	486,698	471,732
Valuation allowance	(477,868)	(462,711)
Total deferred tax assets	8,830	9,021
Deferred tax liabilities:		
Operating lease assets	(8,575)	(8,680)
Prepaid assets	(254)	(341)
Total deferred tax liabilities	(8,830)	(9,021)
Net deferred tax assets (liabilities)	$ —	$ —

The Company follows the accounting guidance related to accounting for income taxes which requires that a company reduce its deferred tax assets by a valuation allowance if, based on the weight of available evidence, it is more likely than not that some portion or all of its deferred tax assets will not be realized. As of December 31, 2021, the Company's deferred tax assets were offset in full by a valuation allowance.

The valuation allowance as of December 31, 2021 increased from $462.7 million to $477.9 million, primarily as a result of additional tax loss generated in various jurisdictions during the current year and the intercompany transfer of intangible assets eligible for tax amortization. Valuation allowances require an assessment of both positive and negative evidence when determining whether it is more likely than not that the deferred tax assets are recoverable. As required, the Company prepares its assessment of the realizability of deferred tax assets on a jurisdiction-by-jurisdiction basis.

As of December 31, 2021, the Company had $305.0 million of US federal net operating loss carryforwards and $24.7 million of federal research and development tax credit carryforwards which expire beginning in 2035. After the enactment of the Tax Cut and Jobs Act (the "Tax Act") in December 2017, the operating losses generated had an indefinite carryforward life, but was limited to 80% of taxable income when utilized. As of December 31, 2021, this amount was $260.1 million. The Company had state net operating loss carryforwards of $90.4 million which generally begin to expire in 2034 and state research and development credit carryforwards of $23.4 million to be carried forward indefinitely.

The Company also had Irish net operating loss carryforwards of $739.6 million with no expiration date and capital loss carryforwards of $58.8 million to be carried forward indefinitely.

Utilization of net operating loss and tax credit carryforwards may be subject to an annual limitation due to ownership change limitations provided by the Internal Revenue Code and similar state provisions. Annual limitations may result in expiration of net operating loss and tax credit carryforwards before some or all of such amounts have been utilized.

The Company's policy is to recognize interest and/or penalties related to income tax matters in income tax expense. The amount of tax expense related to interest or penalties was not material for the year ended December 31, 2021 and 2020.

Uncertain Tax Positions

A reconciliation of the beginning and ending balances of the total amounts of unrecognized tax benefits were as follows:

(In thousands)	
Unrecognized tax benefits as of December 31, 2019	$ 58,763
Gross decrease in tax positions for prior years	(8,059)
Gross increase in tax positions for current year	12,743
Unrecognized tax benefits as of December 31, 2020	63,447
Gross decrease in tax positions for prior years	(395)
Gross increase in tax positions for current year	11,971
Unrecognized tax benefits as of December 31, 2021	$ 75,023

The Company records liabilities related to uncertain tax positions in accordance with the income tax guidance which clarifies the accounting for uncertainty in income taxes recognized in an enterprise's financial statements by prescribing a minimum recognition threshold and measurement attribute for the financial statement recognition and measurement of a tax position taken or expected to be taken in a tax return. Resolution of one or more of these uncertain tax positions in any period may have a material impact on the results of operations for that period. The Company includes any applicable interest and penalties within the provision for income taxes in the consolidated statements of operations.

The total unrecognized tax benefits of $75.0 million and $63.4 million, as of December 31, 2021 and December 31, 2020, respectively, may reduce the effective tax rate in the period of recognition. However, carryforward tax attributes that were generated in years beginning on or before January 1, 2018 may still be adjusted upon examination by tax authorities since the attributes are not yet utilized. The Company does not expect to record any other material reductions in the measurement of its unrecognized tax benefits within the next twelve months. The Company currently has a full valuation allowance against its deferred tax assets, which would impact the timing of the effective tax rate benefit should any of these uncertain positions be favorably settled in the future.

The Company is subject to taxation in Ireland, the US, and various other jurisdictions. The tax years 2018 and forward remain open to examination in Ireland, tax years 2019 and forward remain open to examination in the US, and the tax years 2016 and forward remain open to examination in other jurisdictions.

The Company is currently under Internal Revenue Service ("IRS") examination for the tax year ended December 31, 2018. The Company believes that an adequate provision has been made for any material adjustments that may result from the tax examination. The Company concluded its IRS examination for the tax year ended December 31, 2017 in December 2020 with no adjustments required.

On March 27, 2020, the *Coronavirus Aid, Relief, and Economic Security Act* (the "CARES Act"), that features significant tax provision and other measures to assist individuals and businesses impacted by the economic effects of the COVID-19 pandemic, was signed into law. Tax relief measures for businesses include a five-year net operating loss carryback (including a related technical correction to the 2017 Tax Reform Act), a change in Section 163(j) interest deduction limitations, accelerated alternative minimum tax refunds, payroll tax relief, a temporary suspension of certain aviation excise taxes, a tax credit for employers who retain employees, and a 'qualified improvement property' technical correction to the 2017 Tax Reform Act. The Company has considered the corporate income tax provisions of the CARES Act and related initial guidance as part of its income tax expense and concluded that these provisions did not have a material impact on the Company's 2021 or 2020 income tax expense.

The Company's future income tax expense may be affected by such factors as changes in tax laws, its business, regulations, tax rates, interpretation of existing laws or regulations, the impact of accounting for share-based compensation, the impact of accounting for business combinations, its international organization, shifts in the amount of income before tax earned in the US as compared with other regions in the world, and changes in overall levels of income before tax.

12. Commitments and Contingencies

Performance-Contingent Awards

In 2016, the Compensation Committee granted long-term incentive cash bonus awards to certain employees. The vesting and payout of such awards was dependent on the Company meeting its critical operating goals and objectives during a five-year period from 2016 to December 2020, as well as continued employment. The awards were broken into three separate tranches, and expenses associated with these awards were recognized during the years 2016 to 2021 as the performance conditions were achieved.

The performance conditions associated with the first tranche of the cash bonus awards were completed in the second quarter of 2018, the performance conditions associated with the second tranche were completed in the first quarter of 2019, and the performance conditions associated with the third tranche were completed in the first quarter of 2020. The Company recognized $0.4 million, $3.3 million, and $14.2 million of cash bonus expense for the year ended December 31, 2021, 2020, and 2019, respectively, and the expenses associated with these awards have been fully recognized as of December 31, 2021.

Guarantees and Indemnifications

The Company indemnifies its officers and directors for certain events or occurrences, subject to certain limits. The Company maintains insurance policies that may limit its exposure, and therefore, the Company believes the fair value of these indemnification agreements is minimal. Accordingly, the Company has not recognized any liabilities relating to these agreements as of December 31, 2021. However, no assurances can be given regarding the amounts that may ultimately be covered by the insurers, and the Company may incur substantial liabilities because of these indemnification obligations.

13. Public Offering of Ordinary Shares

On June 29, 2021, the Company sold 6,700,000 ordinary shares at a price to the public of $15.00 per share (the "Shares"). Under the terms of the underwriting agreement, on June 29, 2021, the underwriters also exercised a 30-day option to purchase an additional 1,005,000 ordinary shares for a total of 7,705,000 ordinary shares sold. The total gross proceeds to the Company from the offering were $115.6 million, before deducting underwriting discounts and commissions and offering expenses. The Shares were issued pursuant to the Company's currently effective shelf registration statement on Form S-3 and an accompanying prospectus (File No. 333-235339) filed with the SEC, which became effective automatically on December 3, 2019, and a prospectus supplement filed with the SEC in connection with the offering.

14. Corporate Restructuring

Following unfavorable clinical results related to the Company's late-stage development programs, on September 15, 2021, the Company announced a strategic update and corporate restructuring (the "Restructuring") to focus on leveraging its expertise in developing and commercializing respiratory therapeutics. As part of the Restructuring, the Company initiated a reduction in workforce of approximately 75%, an estimated 270 positions. Approximately 75% of the total reduction in workforce was completed at the end of November 2021, and the remainder will be completed by the end of February 2022.

The Company estimates that it will incur total Restructuring and related expenses of approximately $32.0 million comprised of $17.0 million in cash expenses and $15.0 million in non-cash expenses. These expenses are primarily comprised of severance and other related costs which are being recognized ratably over the future service period.

For the year ended December 31, 2021, the Company incurred Restructuring and related expenses of $20.1 million of which $10.6 million related R&D expenses and $9.5 million related to selling, general and administrative expenses. Of the total $20.1 million, cash-related expenses were $11.5 million and non-cash expenses were $8.6 million which were primarily related to the modification of equity-based awards for employees affected by the Restructuring and certain related awards for other employees.

Selected information relating to accrued cash-related Restructuring expenses was as follows:

(In thousands)	
Balance at December 31, 2020	$ —
Net accruals	11,867
Cash paid	(2,317)
Balance at December 31, 2021	$ 9,550

The Company expects to recognize the majority of the remaining Restructuring and related expenses of approximately $12.0 million, comprised of $5.0 million in cash-related expenses and $7.0 million in non-cash expenses, in the first quarter of 2022 and the balance by the third quarter of 2022. The remaining Restructuring and related expense estimates are subject to a number of assumptions, and actual amounts may differ. The Company may also incur additional costs not currently contemplated due to events that may occur as a result of, or that are associated with, the Restructuring.

The Company also completed an evaluation of the impact of the Restructuring on the carrying value of its long-lived assets, such as property and equipment and operating lease assets. This process includes evaluating the estimated remaining lives, significant changes in the use, and potential impairment charges related to its long-lived assets. Based on its evaluation, the Company determined that its long-lived assets were not impaired as of December 31, 2021, and it did not recognize any impairment charges related to its long-lived assets for the year ended December 31, 2021. The Company may incur additional costs not currently contemplated due to events that may occur because of, or that are associated with, the Restructuring.

SUPPLEMENTARY FINANCIAL DATA
(UNAUDITED)
(In thousands, except per share data)

The following table presents certain unaudited consolidated quarterly financial information for the eight quarters in the periods ended December 31, 2021 and 2020. This information has been prepared on the same basis as the audited consolidated financial statements and includes all adjustments (consisting only of normal recurring adjustments) necessary to present fairly the unaudited quarterly results of operations set forth herein.

	For the Quarter Ended			
	March 31,	June 30,	September 30,	December 31,
2021				
Total revenue	$ 14,257	$ 12,914	$ 13,194	$ 14,946
Costs and expenses	98,149	77,024	66,809	71,113
Loss from operations	(83,892)	(64,110)	(53,615)	(56,167)
Net loss	(79,679)	(52,405)	(35,308)	(32,034)
Basic and diluted net loss per share	$ (1.24)	$ (0.80)	$ (0.48)	$ (0.43)
2020				
Total revenue	$ 19,862	$ 15,008	$ 18,257	$ 18,730
Costs and expenses	92,338	87,184	94,872	95,220
Loss from operations	(72,476)	(72,176)	(76,615)	(76,490)
Net loss	(83,053)	(62,887)	(73,643)	(58,434)
Basic and diluted net loss per share	$ (1.40)	$ (1.00)	$ (1.16)	$ (0.92)

Share of Total YUPELRI Net Sales [(1)]

	For the Quarter Ended			
	March 31,	June 30,	September 30,	December 31,
2021	$ 12,908	$ 14,621	$ 13,806	$ 15,344
2020	$ 12,880	$ 10,589	$ 12,960	$ 13,550

(1) The Company co-promotes YUPELRI in the US under a profit and loss sharing arrangement with Viatris (65% to Viatris; 35% to Theravance Biopharma). The amounts represent the Company's implied 35% share of the total net sales of YUPELRI that were recognized within Viatris' financial statements for the periods presented.

ITEM 9. CHANGES IN AND DISAGREEMENTS WITH ACCOUNTANTS ON ACCOUNTING AND FINANCIAL DISCLOSURE

Not applicable.

ITEM 9A. CONTROLS AND PROCEDURES

Evaluation of Disclosure Controls and Procedures.

We conducted an evaluation required by paragraph (d) of Rule 13a-15 of the Exchange Act as of December 31, 2021, under the supervision and with the participation of our management, including our Chief Executive Officer and Chief Financial Officer, of the effectiveness of the design and operation of our disclosure controls and procedures (as defined under Rule 13a-15(e) of the Exchange Act), which are controls and other procedures of a company that are designed to ensure that information required to be disclosed by a company in the reports that it files under the Exchange Act is recorded, processed, summarized and reported within required time periods. Based upon that evaluation, our Chief Executive Officer and Chief Financial Officer concluded that, as of such date, our disclosure controls and procedures were effective at the reasonable assurance level.

Management's Report on Internal Control over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting, as such term is defined in Rule 13a-15(f) of the Exchange Act. In connection with the preparation of this Annual Report, our management, including our Chief Executive Officer and Chief Financial Officer, assessed the effectiveness of our internal control over financial reporting as of December 31, 2021 based on criteria established in *Internal Control—Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission* (2013 framework) (the "COSO criteria"). Based on its assessment, our management concluded that our internal control over financial reporting was effective as of December 31, 2021.

The effectiveness of our internal control over financial reporting as of December 31, 2021 has been audited by Ernst & Young LLP, an independent registered public accounting firm, as stated in their report which is included herein.

Limitations on the Effectiveness of Controls

Our management, including our Chief Executive Officer and Chief Financial Officer, does not expect that our disclosure controls and procedures or our internal control over financial reporting will prevent all error and all fraud. A control system, no matter how well conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met. Further, the design of a control system must reflect the fact that there are resource constraints, and the benefit of controls must be considered relative to their costs. Because of the inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that all control issues and instances of fraud, if any, within Theravance Biopharma have been detected. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

Changes in Internal Control over Financial Reporting

There was no change in our internal control over financial reporting (as defined in Rule 13a-15(f) of the Exchange Act) identified in connection with the evaluation required by paragraph (d) of Rule 13a-15 of the Exchange Act, which occurred during the fourth quarter of the year ended December 31, 2021 which has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting. We have not experienced any material impact to our internal control over financial reporting despite the fact that many of our employees are working remotely due to the COVID-19 pandemic. We are continually monitoring and assessing the potential impact of COVID-19 on our internal controls to minimize the impact on their design and operating effectiveness.

Report of Independent Registered Public Accounting Firm

To the Shareholders and Board of Directors of Theravance Biopharma, Inc.

Opinion on Internal Control over Financial Reporting

We have audited Theravance Biopharma, Inc.'s internal control over financial reporting as of December 31, 2021, based on criteria established in Internal Control—Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework) (the COSO criteria). In our opinion, Theravance Biopharma, Inc. (the Company) maintained, in all material respects, effective internal control over financial reporting as of December 31, 2021, based on the COSO criteria.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the 2021 consolidated financial statements of the Company and our report dated February 28, 2022 expressed an unqualified opinion thereon, based on our audit and the report of the other auditors as referenced in our report

Basis for Opinion

The Company's management is responsible for maintaining effective internal control over financial reporting and for its assessment of the effectiveness of internal control over financial reporting included in the accompanying Management's Report on Internal Control over Financial Reporting. Our responsibility is to express an opinion on the Company's internal control over financial reporting based on our audit. We are a public accounting firm registered with the PCAOB and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audit in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether effective internal control over financial reporting was maintained in all material respects.

Our audit included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, testing and evaluating the design and operating effectiveness of internal control based on the assessed risk, and performing such other procedures as we considered necessary in the circumstances. We believe that our audit provides a reasonable basis for our opinion.

Definition and Limitations of Internal Control Over Financial Reporting

A company's internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company's internal control over financial reporting includes those policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

/s/ Ernst & Young LLP

Redwood City, California
February 28, 2022

ITEM 9B. OTHER INFORMATION

None.

ITEM 9C. DISCLOSURE REGARDING FOREIGN JURISDICTIONS THAT PREVENT INSPECTIONS

Not applicable.

PART III

ITEM 10. DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE

For the information required by this Item, see “Questions and Answers About Procedural Matters”, “Election of Directors”, “Nominees”, “Audit Committee”, “Meetings of the Board of Directors”, “Code of Conduct”, “Executive Officers” and “Section 16(a) Beneficial Ownership Reporting Compliance” in the Proxy Statement to be filed with the SEC, which sections are incorporated herein by reference.

ITEM 11. EXECUTIVE COMPENSATION

For the information required by this Item, see “Director Compensation”, “Executive Compensation” and “Compensation Committee Interlocks and Insider Participation” in the Proxy Statement to be filed with the SEC, which sections are incorporated herein by reference.

ITEM 12. SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT AND RELATED STOCKHOLDER MATTERS

For the information required by this Item, see “Security Ownership of Certain Beneficial Owners and Management” and “Equity Compensation Plan Information” in the Proxy Statement to be filed with the SEC, which sections are incorporated herein by reference.

ITEM 13. CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS, AND DIRECTOR INDEPENDENCE

For the information required by this Item, see “Director Independence” and “Policies and Procedures for Related Party Transactions” in the Proxy Statement to be filed with the SEC, which sections are incorporated herein by reference.

ITEM 14. PRINCIPAL ACCOUNTANT FEES AND SERVICES

For the information required by this Item, see “Ratification of the Appointment of Independent Registered Public Accounting Firm” and “Pre-Approval of Audit and Non-Audit Services” in the Proxy Statement to be filed with the SEC, which sections are incorporated herein by reference.

PART IV

ITEM 15. EXHIBITS AND FINANCIAL STATEMENT SCHEDULES

(a) The following documents are filed as part of this Annual Report on Form 10-K:

1. Financial Statements:

The following financial statements and schedules of the Registrant are contained in Part II, Item 8, “Financial Statements and Supplementary Data” of this Annual Report on Form 10-K:

2. Financial Statement Schedules:

All schedules have been omitted because of the absence of conditions under which they are required or because the required information, where material, is shown in the financial statements, financial notes or supplementary financial information.

(b) Exhibits required by Item 601 of Regulation S-K

The information required by this Item is set forth on the exhibit index that precedes the signature page of this report.

Exhibit Index

Exhibit Number	Description	Incorporated by Reference	
		Form	Filing Date/Period End Date
2.1	Separation and Distribution Agreement by and between Theravance Biopharma, Inc. and Innoviva, Inc., dated June 1, 2014	8-K	June 3, 2014
2.2*	Asset Purchase Agreement, dated as of November 1, 2018, by and among Cumberland Pharmaceuticals Inc., and Theravance Biopharma Ireland Limited and Theravance Biopharma US, Inc.	8-K	November 16, 2018
3.1	Amended and Restated Memorandum and Articles of Association	10-12B	April 30, 2014
4.1	Specimen Share Certificate	10-12B	April 30, 2014
4.2	Registration Rights Agreement, dated March 3, 2014	10-12B	April 8, 2014
4.3	First Amendment of Registration Rights Agreement, dated February 10, 2020 by and between Theravance Biopharma, Inc. and Glaxo Group Limited	10-Q	March 31, 2020
4.4	Shelf Rights Plan Resolution	DEF 14A	March 21, 2018
4.5	Sales Agreement between Theravance Biopharma, Inc. and Cowen and Company, LLC dated December 3, 2019	S-3	December 3, 2019
4.6	Indenture, dated as of November 2, 2016, between Theravance Biopharma, Inc. and Wells Fargo Bank, National Association, as trustee	8-K	November 2, 2016
4.7	First Supplemental Indenture, dated as of November 2, 2016, between Theravance Biopharma, Inc. and Wells Fargo Bank, National Association, as trustee	8-K	November 2, 2016
4.8	Form of 3.25% Convertible Senior Note due 2023 (included in Exhibit 4.6)	8-K	November 2, 2016
4.9	Indenture, dated as of February 28, 2020, by and among Triple Royalty Sub II LLC, as issuer, U.S. Bank National Association, as initial trustee, transfer agent, paying agent, registrar and calculation agent and, solely with respect to Section 2.11(o) and Section 2.11(p) Theravance Biopharma, Inc.	8-K	March 04, 2020
4.10	Description of the Registrant's Securities Registered Pursuant to Section 12 of the Securities Exchange Act of 1934	10-K	December 31, 2019
4.11	Registration Rights Agreement among Theravance Biopharma, Inc., GSK Finance (No.3) plc and GlaxoSmithKline plc dated June 22, 2020.	8-K	June 25, 2020
4.12	Waiver and Assignment of Registration Rights and Voting Agreement among GSK Finance (No.3) plc, Glaxo Group Limited and Theravance Biopharma, Inc. dated as of June 22, 2020.	8-K	June 25, 2020
10.1	Transition Services Agreement by and between Theravance Biopharma, Inc. and Innoviva, Inc., dated June 2, 2014	8-K	June 3, 2014
10.2	Tax Matters Agreement by and between Theravance Biopharma, Inc. and Innoviva, Inc., dated June 2, 2014	8-K	June 3, 2014
10.3	Employee Matters Agreement by and between Theravance Biopharma, Inc. and Innoviva, Inc., dated June 1, 2014	8-K	June 3, 2014
10.4+	2013 Equity Incentive Plan	S-8	August 18, 2014
10.5+	UK Addendum to the 2013 Equity Incentive Plan	10-Q	August 14, 2014
10.6+	2014 New Employee Equity Incentive Plan	S-8	November 14, 2014
10.7+	2013 Employee Share Purchase Plan, as amended	S-8	Aug. 18, 2014
10.8+	Forms of award agreements under the 2013 Equity Incentive Plan and 2014 New Employee Equity Incentive Plan	10-Q	May 10, 2016
10.9+	Forms of Equity Award Amendment	10-12B	May 7, 2014
10.10+	Form of TFIO Cash Award Amendment	10-12B	May 7, 2014
10.11+	Form of Acknowledgment for Irish Non-Employee Directors	10-K	March 11, 2016

Exhibit Number	Description	Incorporated by Reference	
		Form	Filing Date/Period End Date
10.12+	Irish Addendum to the 2013 Equity Incentive Plan	10-K	March 11, 2016
10.13+	Irish Addendum to the 2014 New Employee Equity Incentive Plan	10-K	March 11, 2016
10.14+	UK and Irish Addendums to the 2013 Employee Share Purchase Plan	10-K	March 11, 2016
10.15+	Theravance Biopharma, Inc. Performance Incentive Plan	8-K	May 6, 2016
10.16+	Form of Notice of Option Grant and Option Agreement under the Company's Performance Incentive Plan	10-Q	November 8, 2017
10.17+	Form of Notice of Performance Restricted Share Unit Award and Restricted Share Unit Agreement under the Company's Performance Incentive Plan	10-Q	November 8, 2017
10.18+	Change in Control Severance Plan	10-12B	April 8, 2014
10.19+	Cash Bonus Program	10-12B	November 22, 2013
10.20+	Form of Indemnity Agreement	10-12B	April 30, 2014
10.21	Amended and Restated Lease Agreement, 951 Gateway Boulevard, between Innoviva, Inc. and HMS Gateway Office L.P., dated January 1, 2001	10-12B	August 1, 2013
10.22	First Amendment to Lease for 951 Gateway Boulevard effective as of June 1, 2010 between Innoviva, Inc. and ARE-901/951 Gateway Boulevard, LLC	10-12B	August 1, 2013
10.23	Lease Agreement, 901 Gateway Boulevard, between Innoviva, Inc. and HMS Gateway Office L.P., dated January 1, 2001	10-12B	August 1, 2013
10.24	First Amendment to Lease for 901 Gateway Boulevard effective as of June 1, 2010 between Innoviva, Inc. and ARE-901/951 Gateway Boulevard, LLC	10-12B	August 1, 2013
10.25	Consent to Assignment by and among ARE-901/951 Gateway Boulevard, LLC, Innoviva, Inc. and Theravance Biopharma, Inc. and Assignment and Assumption of Lease for 901 Gateway Blvd.	10-Q	August 14, 2014
10.26	Consent to Assignment by and among ARE-901/951 Gateway Boulevard, LLC, Innoviva, Inc. and Theravance Biopharma, Inc. and Assignment and Assumption of Lease for 951 Gateway Blvd.	10-Q	August 14, 2014
10.27	Theravance Respiratory Company, LLC Limited Liability Company Agreement, dated May 31, 2014	8-K	June 3, 2014
10.28*	Technology Transfer and Supply Agreement, dated as of May 22, 2012 between Innoviva, Inc. and Hospira Worldwide, Inc.	10-12B	May 7, 2014
10.29*	First Amendment to the Technology Transfer and Supply Agreement by and between Innoviva, Inc. and Hospira Worldwide, Inc., dated May 16, 2013	10-Q	November 9, 2016
10.30*	Second Amendment to the Technology Transfer and Supply Agreement by and between Theravance Biopharma Antibiotics, Inc. and Hospira Worldwide, Inc., dated October 17, 2014	10-Q	November 9, 2016
10.31*	Third Amendment to the Technology Transfer and Supply Agreement by and between Theravance Biopharma Ireland Limited and Hospira Worldwide, Inc., dated April 14, 2016	10-Q	November 9, 2016
10.32*	Fourth Amendment to the Technology Transfer and Supply Agreement by and between Theravance Biopharma Ireland Limited and Pfizer CentreOne group of Pfizer, Inc., dated September 29, 2016	10-Q	November 9, 2016
10.33	Amendment No. 1 to the License, Development, and Commercialization Agreement by and between Theravance Biopharma Ireland Limited and Clinigen Group PLC dated August 4, 2016	10-Q	August 9, 2016
10.34	License Agreement with Janssen Pharmaceutica, dated as of May 14, 2002	10-Q	August 14, 2014
10.35	Collaboration Agreement between Innoviva, Inc. and Glaxo Group Limited, dated November 14, 2002 (1)		
10.36	Strategic Alliance Agreement by and between Innoviva, Inc. and Glaxo Group Limited, dated March 30, 2004 (2)		
10.37	Amendment to Strategic Alliance Agreement by and between Innoviva, Inc. and Glaxo Group Limited, dated October 3, 2011 (3)		

Exhibit Number	Description	Incorporated by Reference	
		Form	Filing Date/Period End Date
10.38	Collaboration Agreement Amendment by and between Innoviva, Inc. and Glaxo Group Limited dated, March 3, 2014 (4)		
10.39	Strategic Alliance Agreement Amendment by and between Innoviva, Inc. and Glaxo Group Limited dated, March 3, 2014 (4)		
10.40	Master Agreement by and between Innoviva, Inc., Theravance Biopharma, Inc. and Glaxo Group Limited, dated March 3, 2014 (4)		
10.41	Extension Agreement by and between the Company and Glaxo Group Limited, dated March 3, 2014	10-12B	April 8, 2014
10.42+	Amended Offer Letter with Rick E Winningham dated August 5, 2014	10-Q	November 12, 2014
10.43+	Offer Letter with Frank Pasqualone May 12, 2014	10-Q	August 14, 2014
10.44+	Offer Letter with Brett K. Haumann dated May 12, 2014	10-Q	August 14, 2014
10.45+	Offer Letter with Brad Shafer dated August 20, 2014	10-Q	November 12, 2014
10.46+	Offer Letter with Ken Pitzer September 15, 2014	10-Q	May 10, 2016
10.47+	Offer Letter with Phil Worboys September 9, 2014	10-Q	May 10, 2016
10.48+	Offer Letter with Richard Graham, Ph.D. dated August 12, 2015	10-Q	September 30, 2020
10.49**	Development and Commercialization Agreement by and between Theravance Biopharma R&D, Inc. and Mylan Ireland Limited, dated January 30, 2015	10-K	December 31, 2020
10.50*	License and Collaboration Agreement by and between Theravance Biopharma Ireland Limited and Millennium Pharmaceuticals, Inc. dated June 8, 2016	10-Q	August 9, 2016
10.51	Form of Note Purchase Agreement, dated February 21, 2020 by and among Theravance Biopharma R&D, Inc., Triple Royalty Sub II LLC, and the Purchasers	10-K	December 31, 2019
10.52	Sale and Contribution Agreement, dated as of February 28, 2020, among Theravance Biopharma R&D, Inc., as the transferor, Triple Royalty Sub II LLC, as the transferee, and Theravance Biopharma, Inc.	8-K	March 04, 2020
10.53	Pledge and Security Agreement, dated as of February 28, 2020, between Theravance Biopharma R&D, Inc., as the equity holder, and U.S. Bank National Association, as the trustee	8-K	March 04, 2020
10.54	Servicing Agreement, dated as of February 28, 2020, between Triple Royalty Sub II LLC and Theravance Biopharma US, Inc.	8-K	March 04, 2020
10.55	Account Control Agreement, dated as of February 28, 2020, among Triple Royalty Sub II LLC, as the grantor, Theravance Biopharma US, Inc., as the servicer, U.S. Bank National Association, as the secured party, and U.S. Bank National Association, as the financial institution	8-K	March 04, 2020
10.56	Amended and Restated Limited Liability Company Agreement of Triple Royalty Sub II LLC, dated February 28, 2020, by Theravance Biopharma R&D, Inc., as the initial sole equity member	8-K	March 04, 2020
10.57	Annex A - Rules of Construction and Defined Terms of the Amended and Restated Limited Liability Company Agreement of Triple Royalty Sub II LLC, dated February 28, 2020	8-K	March 04, 2020
10.58**	License and Collaboration Agreement by and between Theravance Biopharma Ireland Limited and Janssen Biotech, Inc. dated as of February 5, 2018	10-K	December 31, 2020
10.59+	Memorandum to Brett K. Haumann regarding Transfer to Transfer to Theravance Biopharma UK Limited, executed April 1, 2020	10-Q	March 31, 2020
10.60	Amendments to Lease for 901 Gateway Boulevard between Theravance Biopharma US, Inc. and ARE-901/951 Gateway Boulevard, LLC	10-Q	August 2, 2018
10.61	Amendments to Lease for 951 Gateway Boulevard between Theravance Biopharma US, Inc. and ARE-901/951 Gateway Boulevard, LLC	10-Q	August 2, 2018
10.62+	Agreement and General Release between Theravance Biopharma US, Inc. and Shehnaaz Suliman, dated March 1, 2019	10-Q	May 10, 2019
10.63+	Offer Letter with Andrew Hindman dated May 30, 2019	10-Q	August 5, 2019

Exhibit Number	Description	Incorporated by Reference	
		Form	Filing Date/Period End Date
10.64*	Amendment No. 1 to the Development and Commercialization Agreement by and between Theravance Biopharma Ireland Limited and Mylan Ireland Limited, dated June 12, 2019	10-Q	August 5, 2019
10.65**	License Agreement by and between Theravance Biopharma Ireland Limited and Pfizer Inc. dated December 21, 2019	10-K	December 31, 2019
10.66+	Service Agreement by and between Brett K. Haumann and Theravance Biopharma UK Limited, dated April 1, 2020	10-Q	March 31, 2020
10.67	Cooperation Agreement among Theravance Biopharma, Inc., GSK Finance (No.3) plc and GlaxoSmithKline plc, dated June 22, 2020	8-K	June 25, 2020
10.68+	Consulting Agreement between Bradford J. Shafer and Theravance Biopharma, Inc., dated September 30, 2021	8-K	October 15, 2021
10.69+	Form of Separation Agreement and Release of Claims between California-based departing executives and Theravance Biopharma US, Inc.		
10.70+	Consulting Agreement between Vijay Sabesan and Theravance Biopharma US, Inc., dated November 30, 2021		
10.71+	Settlement Agreement by and between Ann Brady and Theravance Biopharma Ireland Limited, dated November 2, 2021		
10.72	Audited financial statements of Theravance Respiratory Company, LLC for the year ended December 31, 2021		
21.1	Subsidiaries of Theravance Biopharma, Inc.		
23.1	Consent of Independent Registered Public Accounting Firm (Ernst & Young LLP)		
23.2	Consent of Independent Registered Public Accounting Firm (Grant Thornton LLP)		
24.1	Power of Attorney (see signature page to this Annual Report on Form 10-K)		
31.1	Certification of Chief Executive Officer Pursuant to Rule 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934		
31.2	Certification of Chief Financial Officer Pursuant to Rule 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934		
32	Certifications Pursuant to 18 U.S.C. Section 1350		
101	The following materials from Registrant's Annual Report on Form 10-K for the year ended December 31, 2021, formatted in Inline Extensible Business Reporting Language (iXBRL) includes: (i) Consolidated Balance Sheets, (ii) Consolidated Statements of Operations, (iii) Consolidated Statements of Comprehensive Loss, (iv) Consolidated Statements of Shareholders' Deficit, (v) Consolidated Statements of Cash Flows, and (vi) Notes to Consolidated Financial Statements.		
104	Cover Page Interactive Data File (Formatted as Inline XBRL and contained in Exhibit 101).		

+ Management contract or compensatory plan or arrangement required to be filed pursuant to Item 15(b) of Form 10-K.

* Portions of this exhibit have been omitted and the omitted information has been filed separately with the Securities and Exchange Commission pursuant to an order granting confidential treatment.

** Portions of this exhibit have been omitted pursuant to Item 601(b)(10)(iv) of Regulation S-K.

(1) Incorporated by reference to an exhibit filed with the quarterly report on Form 10-Q of Innoviva, Inc., filed with the Securities and Exchange Commission on August 7, 2014.

(2) Incorporated by reference to an exhibit filed with the annual report on Form 10-K of Innoviva, Inc., filed with the Commission on March 3, 2014.

(3) Incorporated by reference to an exhibit filed with the annual report on Form 10-K of Innoviva, Inc., filed with the Commission on February 27, 2012.

(4) Incorporated by reference to an exhibit filed with the current report on Form 8-K/A of Innoviva, Inc., filed with the Commission on March 6, 2014.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the Registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

THERAVANCE BIOPHARMA, INC.

Date: February 28, 2022

By: /s/ Rick E Winningham
Rick E Winningham
Chief Executive Officer

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Rick E Winningham as their true and lawful attorney-in-fact and agent, each with full power of substitution and resubstitution, for such person and in his or her name, place and stead, in any and all capacities, to sign any and all amendments to the annual report on Form 10-K, and to file the same, with all exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorney-in-fact and agent full power and authority to do and perform each and every act and thing requisite and necessary to be done in and about the premises, as fully to all intents and purposes as he or she could do in person, hereby ratifying and confirming all that said attorney-in-fact and agent, or his substitute, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed below by the following persons on behalf of the registrant and in the capacities and on the dates indicated.

Signature	Title	Date
/s/ Rick E Winningham Rick E Winningham	Chairman of the Board and Chief Executive Officer (Principal Executive Officer)	February 28, 2022
/s/ Andrew Hindman Andrew Hindman	Senior Vice President and Chief Financial Officer (Principal Financial Officer)	February 28, 2022
/s/ Laurie Smaldone Alsup, M.D. Laurie Smaldone Alsup, M.D.	Director	February 28, 2022
/s/ Eran Broshy Eran Broshy	Director	February 28, 2022
/s/ Donal O'Connor Donal O'Connor	Director	February 28, 2022
/s/ Burton G. Malkiel, Ph.D. Burton G. Malkiel, Ph.D.	Director	February 28, 2022
/s/ Dean J. Mitchell Dean J. Mitchell	Director	February 28, 2022

Signature	Title	Date
/s/ Susan M. Molineaux, Ph.D. Susan M. Molineaux, Ph.D.	Director	February 28, 2022
/s/ Deepika R. Pakianathan, Ph.D. Deepika R. Pakianathan, Ph.D.	Director	February 28, 2022
/s/ William D. Young William D. Young	Director	February 28, 2022

SEPARATION AGREEMENT AND RELEASE OF CLAIMS

This Separation Agreement and Release of Claims ("Agreement") is made and entered into by and between [_____] ("Employee") and Theravance Biopharma US, Inc. ("Theravance" or "Company"). Employee and Theravance shall be referred to herein as the "Parties."

Employee's employment with Theravance terminated on November 30, 2021 (the "Termination Date") in connection with a reduction in force. When this Agreement becomes effective as set forth in paragraph K it will constitute the agreement to provide severance benefits to Employee in exchange for Employee entering this Agreement which among other things includes a release of claims.

Employee and Theravance agree as follows:

A. Severance Benefits

After this Agreement becomes effective pursuant to paragraph K Theravance shall provide Employee with the following severance benefits:

1. **Severance Payment:** Following the Termination Date, Theravance will pay Employee a lump sum equivalent to twelve (12) weeks of Employee's base salary as of November 29, 2021, which equals the gross amount of $[_____] and which will be subject to all applicable taxes, deductions, and other withholdings.

2. **Health Insurance Continuation:** Provided Employee completes the required documentation to continue Employee's health insurance coverage under COBRA Theravance will pay the cost of continuing Employee's health insurance coverage under COBRA for up to 9 months at the level of coverage applicable to the employee on the Termination Date. COBRA coverage payment by Theravance will cease if Employee obtains other health insurance coverage during the period Employee is eligible for Theravance paid coverage under the terms of this Agreement. Employee agrees to notify Theravance in the event Employee obtains other health insurance coverage. Employee will be responsible for making payments to continue health insurance under COBRA after the period for which Theravance is paying the cost under the terms of this Agreement.

3. **Acceleration of Vesting:** The treatment of Employee's outstanding equity awards to acquire ordinary shares of Theravance Biopharma, Inc. shall be governed by the applicable award agreement and plan rules, including but not limited to the Theravance Biopharma, Inc. 2013 Equity Incentive Plan or other applicable equity incentive plan. To the extent permissible under the rules of any applicable plans, and subject to strict compliance by Employee with Employee's obligations hereunder, Employee's outstanding unvested restricted share unit ("RSU") awards that would have vested over the next three (3) fiscal quarters following the Termination Date (*i.e.*, on February 20, 2022, May 20, 2022, and August 20, 2022) had Employee remained employed by the Company through such dates will benefit

from accelerated vesting and will vest as of the effective date of this Agreement (the "Vesting Acceleration"). To the extent any RSUs vest pursuant to this paragraph A.3, the date the RSUs will be settled will be on a date or dates to be selected by the Company in its sole discretion (no later than March 15, 2022). The date the RSUs will be settled will depend on when the Agreement becomes effective, compliance with securities laws, compliance with the equity plan documents, internal administrative considerations and potential restrictions on Theravance's ability to carry out the settlement of RSUs. The Employee acknowledges and agrees that, effective as of the Termination Date, the "tax withholding obligations" (as defined in Employee's restricted share unit agreement(s)) applicable to Employee's RSUs may no longer be satisfied by withholding of shares. To the extent any RSUs vest pursuant to this paragraph A.3, the Company will instruct E*Trade to sell a number of shares subject to Employee's RSUs necessary to satisfy Company's minimum statutory tax withholding requirements (with the remaining shares deposited into Employee's E*Trade account), consistent with the "sell to cover" instructions Employee provided to the Company. While Theravance will seek to settle RSUs without undue delay, Employee is informed that RSUs may ultimately not be settled until the Company's open trading window in the first quarter 2022 (though in any event no later than March 15, 2022). Employee acknowledges and agrees that except as set forth in this paragraph, vesting of Employee's outstanding equity awards will cease on the Termination Date and that no further vesting will occur other than pursuant to the Theravance Biopharma, Inc. Change in Control Severance Plan ("Severance Plan").

4. **Change in Control Severance Benefits:** To the extent Theravance Biopharma, Inc. is subject to a "Change in Control" (as defined in the Severance Plan) within three months after the Termination Date, Employee will be eligible for the severance benefits described in the Severance Plan on the terms and conditions set forth therein; provided, however, that such severance benefits shall be reduced by any amounts paid to or on account of Employee pursuant to paragraphs A.1. and A.2. hereof.

B. Release of Claims by Employee

1. General Release and Releasees:

Except as set forth below, in consideration of the severance benefits provided herein, Employee on Employee's behalf, and on behalf of Employee's agents, heirs, beneficiaries and assigns, hereby fully and forever releases, waives, discharges and promises not to sue or otherwise maintain, institute or cause to be instituted any legal proceedings against Theravance, or its related entities and subsidiaries, or any of its or its related entities' and subsidiaries' current or former officers, directors, shareholders, predecessors, successors, agents, employees, contractors, insurers, representatives, joint employers, or any person or entity to which Theravance has provided services (collectively, "Releasees"), with respect to any and all liabilities, claims, demands, contracts, debts, monetary damages or other form of personal relief, of any nature, kind and description, whether at law, in equity or

otherwise, whether or not now known or ascertained, which currently do or may exist, including without limitation any matter, cause or claim arising out of or related to any and all acts, events or omissions, occurring prior to the date this Agreement is executed (collectively "Released Claims").

2. Claims Covered by General Release:

Except as set forth herein, the Released Claims include, but are not limited to, those that have been or could be asserted against any Releasee arising out of, in connection with, or in any way related to (a) Employee's employment with, or separation from, Theravance; (b) any term or condition of Employee's employment with Theravance, including but not limited to any and all disputed wages, compensation, salaries, commissions, pay, allowances, monies, expenses/reimbursements, employee benefits, sick/vacation pay, paid leave benefits, any other disputed wage and hour related claims, and any other benefits, penalties, interest, damages, and promises related to the same; and (c) any claims to any equity interest in Theravance, including without limitation stock options, shadow stock, restricted stock, membership units, distribution rights, partnership, stock, and all other forms of equity, except as addressed in paragraph A.3.

Without limiting the foregoing, by way of example only and except as set forth herein, the Released Claims also include any and all claims for severance benefits, attorneys' fees, indemnification, injunctive relief, breach of contract, promissory estoppel, quantum meruit, breach of the covenant of good faith and fair dealing, violation of public policy, intentional or negligent infliction of emotional distress, intentional or negligent misrepresentation, fraud, defamation, negligent hiring/supervision, assault/battery, constructive discharge, wrongful discharge, retaliation, claims under Title VII of the Civil Rights Act of 1964, the Civil Rights Act of 1964, the Private Attorneys General Act of 2004 ("PAGA"), the Civil Rights Act of 1866, the Americans with Disabilities Act, the Unruh Act, the Family and Medical Leave Act, the Worker Adjustment and Retraining Notification Act, the Older Workers Benefit Protection Act, the Age Discrimination in Employment Act, the California Fair Employment and Housing Act, the California Labor Code, California Wage Orders, the California Business and Professions Code, the California Family Rights Act, the Pregnancy Disability Leave law, the California Constitution, [the Pennsylvania Human Relations Act, the Pennsylvania Equal Pay Law, the Pennsylvania Minimum Wage Act,] and any other statutory, regulatory or common law claims relating to employment.

Except as set forth herein, all Released Claims are forever waived and barred by this Agreement regardless of the forum in which they may be brought. The Parties intend for this release to be as broad as legally permissible.

C. Waiver of Unknown Claims – Civil Code Section 1542

In furtherance of the intent to waive, release and discharge Theravance from any and all Released Claims, whether known or unknown, Employee understands and agrees that except as set forth herein the Release stated in paragraph B applies to claims known and presently unknown by Employee; and that this means that if, hereafter, Employee discovers

facts different from or in addition to those which Employee now knows or believes to be true, that the release and waiver in paragraph B shall be and remain effective in all respects notwithstanding such different or additional facts or the discovery of such facts.

Accordingly, Employee hereby expressly and knowingly waives, fully and forever, any and all rights and benefits conferred upon Employee by the provisions of Section 1542 of the Civil Code of the State of California and any statutes or legal principles of like effect of any other jurisdiction. Civil Code Section 1542 states:

> **A GENERAL RELEASE DOES NOT EXTEND TO CLAIMS THAT THE CREDITOR OR RELEASING PARTY DOES NOT KNOW OR SUSPECT TO EXIST IN HIS OR HER FAVOR AT THE TIME OF EXECUTING THE RELEASE AND THAT, IF KNOWN BY HIM OR HER, WOULD HAVE MATERIALLY AFFECTED HIS OR HER SETTLEMENT WITH THE DEBTOR OR RELEASED PARTY.**

D. Matters Excluded From Released Claims

Notwithstanding the terms of paragraphs B and C, nothing contained in this Agreement shall be deemed to be a release or waiver by Employee of any claim which cannot be waived or released by private agreement. In addition, the Released Claims in Paragraph B hereof shall not include: (a) any benefit entitlements vested as of the date Employee's employment ended, including pursuant to written terms of any applicable employee benefit plan governed by the Employment Income Security Act of 1974 ("ERISA"); (b) rights under Workers' Compensation or Unemployment Insurance law; (c) rights under the Theravance Biopharma, Inc. Change in Control Severance Plan except as limited in paragraph A.4; [or] (d) rights arising under this Agreement[; or (e) claims under the Pennsylvania Wage Payment and Collection Law and Pennsylvania Worker and Community Right-to-Know Act].

This Agreement shall not prohibit Employee from filing a claim with a government agency that is responsible for enforcing a law such as the Securities and Exchange Commission ("SEC"), the National Labor Relations Board ("NLRB"), the Equal Employment Opportunity Commission ("EEOC"), the Department of Fair Employment and Housing ("DFEH"), the Office of Federal Contract Compliance Programs ("OFCCP") or the Occupational Safety and Health Administration ("OSHA"). However, unless subject to legal requirements to the contrary, if any, Employee understands that by entering this Agreement, Employee will not be entitled to recover any monetary damages or any other form of personal relief in connection with such a claim, investigation or proceeding.

This Agreement shall not be construed to prohibit Employee from providing information regarding Employee's former employment relationship with Theravance as may be required by law or legal process, or from cooperating, participating or assisting in any government or regulatory entity investigation or proceeding.

E. Proprietary Information

Employee acknowledges that Employee signed the Theravance Biopharma US, Inc. Proprietary Information and Inventions Agreement ("PIIA") in connection with Employee's employment with Theravance. Employee represents that Employee has not breached the PIIA, including but not limited to by retaining possession or control of any Proprietary Information, Company Documents and/or other Theravance materials, or causing another person or persons to retain possession or control of Proprietary Information, Company documents and/or other Theravance materials, in violation of the PIIA. Employee understands that the terms of the PIIA survive the termination of Employee's employment and shall remain binding and enforceable against Employee. Notwithstanding anything herein to the contrary, an individual shall not be held criminally or civilly liable under any Federal or State trade secret law for the disclosure of a trade secret that (A) is made (i) in confidence to a Federal, State, or local government official, either directly or indirectly, or to an attorney; and (ii) solely for the purpose of reporting or investigating a suspected violation of law; or (B) is made in a complaint or other document filed in a lawsuit or other proceeding, if such filing is made under seal. An individual who files a lawsuit for retaliation by an employer for reporting a suspected violation of law may disclose the trade secret to the attorney of the individual and use the trade secret information in the court proceeding, if the individual (A) files any document containing the trade secret under seal; and (B) does not disclose the trade secret, except pursuant to court order. Nothing herein is intended, or should be construed, to affect the immunities created by the Federal Defend Trade Secrets Act of 2016 or any similar state law.

If Employee does not possess a copy of the PIIA that Employee signed, a copy may be obtained by contacting Charissa Shaughnessy, cshaughnessy@theravance.com, (650) 465-4546.

F. Governing Law

The Parties hereby agree that California law shall govern the construction, interpretation and enforcement of this Agreement.

G. Severability

The Parties agree that if any provision, or portion thereof, of this Agreement shall for any reason be determined to be invalid, unenforceable or contrary to public policy or any law, it shall if possible be interpreted, modified or reformed as necessary to be enforceable. If it cannot be interpreted, modified or reformed to be enforceable, such provision or portion thereof that is determined to be invalid, unenforceable, contrary to public policy or law shall be severed and deemed null and void, leaving the remainder of this Agreement in force and effect as a separation agreement and release of claims.

H. Consideration Period

Employee will have forty-five (45) days from November 30, 2021 within which to consider this Agreement and to decide whether to enter it; however, Employee is free to execute it at any time before the expiration of the consideration period. Employee is hereby advised

to consult with an attorney regarding this Agreement; however, Employee is not required to do so.

I. Signing Agreement

If Employee decides to enter this Agreement, it must be signed electronically by completing the DocuSign process linked on the signature line on page 7. Agreements signed and accepted by the DocuSign process will be automatically forwarded to Theravance.

J. Revocation

Employee will have seven (7) days following Employee's signing of this Agreement to revoke Employee's acceptance of it. To revoke, Employee must deliver a written statement of revocation to Charissa Shaughnessy, cshaughnessy@theravance.com by e-mail or mail or delivery of a physical document addressed to Charissa Shaughnessy, 901 Gateway Boulevard, South San Francisco, CA 94080, no later than midnight on the seventh (7th) day after Employee signed this Agreement. If Employee revokes within seven (7) days, Employee will receive no benefits under this Agreement.

K. Effective Date

If Employee signs and does not exercise Employee's right to revoke this Agreement, it shall become effective on the eighth day after Employee signs it. The severance payment provided for herein shall be paid to Employee on or by the normal Theravance payday following the next payday after the Agreement becomes effective. COBRA payment and coverage will become effective retroactive to December 1, 2021 if Employee completes the required COBRA documentation. Settlement of RSUs and Vesting Acceleration will take place as set forth in paragraph A.3. Receipt of severance benefits is expressly conditioned on Employee's compliance with the terms of this Agreement, and return of all Theravance property, except for Theravance property Employee receives written permission to retain.

L. Additional Information

Attached hereto as Exhibit 1 is information Theravance is required to provide under the Older Worker Benefit Protection Act in connection with Employee's release of rights under the Age Discrimination in Employment Act. Exhibit 1 lists the job titles, ages, and dates of termination for employees selected for inclusion in the reduction in force and eligible for severance benefits, and the job titles and ages of employees considered but not selected for inclusion in the reduction in force who are ineligible for severance benefits.

M. Effect of Agreement

This Agreement, once it has been executed by Employee and has become effective and fully enforceable, will be a full and complete defense to any action or proceeding initiated or prosecuted by Employee concerning rights released and waived herein. If Employee

does not sign this Agreement or revokes Employee's acceptance after signing Employee will not receive the severance benefits set forth in paragraph A.

N. Entire Agreement

This Agreement constitutes the entire agreement between the Parties regarding the matters set forth herein, and no amendment or modification will be effective unless in writing and signed by the party against whom enforcement is sought. This Agreement supersedes and replaces all agreements currently in effect between Employee and Theravance regarding the subjects addressed herein, except for those agreements expressly identified herein as continuing in effect.

I knowingly and voluntarily agree to the terms of this Agreement.

Dated: _____

By: _____
Signature

_____
Print Name

Dated: November 30, 2021

Theravance Biopharma US, Inc.

CONSULTING AGREEMENT

Effective November 30, 2021 (the "Effective Date"), Vijay Sabesan ("Consultant") and Theravance Biopharma US, Inc. ("Theravance Biopharma" or the "Company") agree as follows:

1. Services and Payment. Consultant agrees to consult with and advise Theravance Biopharma from time to time, at Theravance Biopharma's request and as reasonably agreed to by the parties ("Services"). Services and the compensation related thereto to be provided hereunder are set forth in Exhibit A attached hereto. Consultant shall also be entitled to reimbursement for reasonable expenses such as costs for hotel, transportation and meals incurred in connection with the Services and which Consultant has received prior approval from Theravance within thirty (30) days of Consultant's submission of receipts thereof.

2. Ownership of Inventions. Theravance Biopharma shall own all legal right, title and interest (including patent rights, copyrights, trade secret rights, trademark rights and all other rights of any sort throughout the world) relating to any and all inventions (whether or not patentable), including without limitation, discoveries, compositions of matter, pharmaceutical formulations, methods of use, methods of making, techniques, processes, formulas, improvements, works of authorship, designations, designs, know-how, ideas and information made or conceived or reduced to practice, in whole or in part, by Consultant (solely or jointly with others) during the term of this Agreement that arise out of or relate to the Services or any Proprietary Information (as defined below) (collectively, "Inventions"). Consultant hereby does assign all Inventions to Theravance Biopharma and agrees to promptly disclose and provide all such Inventions to Theravance Biopharma. Consultant shall further assist Theravance Biopharma, at Theravance Biopharma's expense, to further evidence, record and perfect such assignments, and to perfect, obtain, maintain, enforce, and defend any rights assigned throughout the world. Such assistance may include, but is not limited to, execution of documents and assistance or cooperation in legal proceedings. Consultant hereby irrevocably designates and appoints Theravance Biopharma as Consultant's agent and attorney-in-fact to act for and on Consultant's behalf to execute and file any document and to do all other lawfully permitted acts to further the foregoing with the same legal force and effect as if executed by Consultant. When requested by Theravance Biopharma, Consultant will make available to Theravance Biopharma all notes, data and other information relating to any Invention.

3. Proprietary Information. Consultant agrees that all Inventions and other business, technical and financial information concerning Theravance Biopharma (including, without limitation, the identity of and information relating to employees, vendors and service providers of Theravance Biopharma and its affiliates) that Consultant develops, learns or obtains during the term of this Agreement or while Consultant is providing Services constitute "Proprietary Information." Consultant will hold in confidence and not disclose or make available to third parties or make use of any Proprietary Information except with the prior written consent of Theravance Biopharma or to the extent necessary in performing Services for Theravance Biopharma. However, Consultant shall not be obligated under this paragraph with respect to information Consultant can document (i) is or becomes readily publicly available without restriction through no fault of Consultant, or (ii) that Consultant knew without restriction prior to its disclosure by Theravance Biopharma. Upon termination of this Agreement or as otherwise requested by Theravance Biopharma, Consultant will promptly return to Theravance Biopharma all documents, materials and copies containing or embodying Proprietary Information, except that Consultant may keep a personal copy of (i) compensation records relating to the Services and (ii) this Agreement.

4. Solicitation. As additional protection for Proprietary Information, Consultant agrees that during the term of this Agreement and for one year thereafter, Consultant will not encourage or solicit any employee of or consultant to Theravance Biopharma or any of its affiliates to leave Theravance Biopharma or any of its affiliates for any reason. In the event that Consultant receives an unsolicited request from an employee of Theravance Biopharma seeking employment opportunities outside of Theravance Biopharma, it will not be a breach of this provision for Consultant to redirect such inquiry to

a third party provided Consultant does not actively participate in any discussion or activity regarding such inquiry beyond provision of a reference for such employee.

5. Term. This Agreement shall become effective on the Effective Date and remain in force until February 28, 2022. All provisions of this Agreement and any remedies for breach of this Agreement shall survive expiration.

6. Relationship of the Parties. Notwithstanding any provision hereof, for all purposes of this Agreement each party shall be and act as an independent contractor and not as a partner, joint venturer, or agent of the other and shall not bind nor attempt to bind the other to any contract. Consultant is an independent contractor and not an employee of Theravance Biopharma and, as such, is solely responsible for all taxes, withholdings, and other statutory or contractual obligations of any sort, including, but not limited to, Workers' Compensation Insurance. Consultant and Theravance Biopharma agree that Theravance Biopharma shall have no authority to control or direct how Consultant performs the Services and it shall be the responsibility solely of Consultant to ensure Consultant performance the Services in accordance with the commitments it is making in this Agreement. Consultant recognizes and agrees that Consultant has no expectation of privacy with respect to Theravance Biopharma's telecommunications, networking or information processing systems (including, without limitation, computer files, email messages and attachments, and voice messages) and that Consultant's activity, and any files or messages, on or using any of those systems may be monitored at any time without notice.

7. Assignment. This Agreement and the Services performed hereunder are personal to Consultant and Consultant shall not have the right or ability to assign, transfer, or subcontract any obligations under this Agreement without the written consent of Theravance Biopharma. Any attempt to do so shall be void. Theravance Biopharma shall be free to assign or transfer this Agreement to a third party.

8. Representations. Consultant represents and warrants that:

8.1 Consultant has never been: (1) debarred, excluded or convicted of a crime for which a person can be debarred under 21 U.S.C. § 335a; (2) excluded by the OIG or other government entity as listed on http://exclusions.oig.hhs.gov/ or www.sam.gov; or (3) threatened to be debarred, excluded or indicted for a crime or otherwise engaged in conduct for which a person can be debarred, excluded or indicted. Consultant agrees to notify Theravance Biopharma in writing immediately in the event of any such debarment, exclusion, conviction, threat or indictment occurring during the term of this Agreement, or the three (3) year period following the termination or expiration of this Agreement;

8.2 If at any time during the term of this Agreement, Consultant becomes the subject of any proceedings for disqualification, debarment, delisting, exclusion, or denial or revocation of licensure, as described above, Theravance Biopharma shall have the right to terminate this Agreement effective upon the date of such notice by Consultant; and

8.3 (i) Consultant's performance hereunder will not breach any agreement or obligation to keep in confidence proprietary information acquired by Consultant in confidence or trust prior to or during Consultant's engagement with Theravance Biopharma, and (ii) all work under this Agreement will be Consultant's original work and none of the Services or Inventions or any development, use, production, distribution or exploitation thereof will infringe, misappropriate or violate any intellectual property or other right of any person or entity. Consultant represents and warrants that Consultant has not entered into, and agrees that Consultant will not enter into, any agreement whether written or oral in conflict with this Agreement or with Consultant's obligations as a consultant to Theravance Biopharma. Consultant represents and warrants that Consultant will not use any funds or facilities of Consultant's employing entit(ies) in the performance of the Services.

9. Company Policies. Consultant represents Consultant has read the Theravance Biopharma, Inc. Insider Trading Policy and the Theravance Biopharma, Inc. Code of Business Conduct and shall abide by the applicable portions of such Policy and such Code in performing the Services.

10. Maintenance of Records. Consultant shall maintain complete files and records of all Services provided on behalf of Theravance Biopharma hereunder and the cost of any materials paid for by Consultant in connection with providing such Services. Upon Theravance Biopharma's request, Consultant shall provide Theravance Biopharma with the above-mentioned documents within forty-five (45) days. Theravance Biopharma and/or any audit firm engaged by Theravance Biopharma shall have the right, at no additional charge, upon reasonable notice, to examine such records, including supporting documentation, throughout the term of this Agreement, and after termination of this Agreement pending resolution of any disputes between Theravance Biopharma and Consultant.

11. Remedies. Any breach of Section 2, 3, 4, 8, 9 or 10 will cause irreparable harm to Theravance Biopharma for which damages would not be an adequate remedy, and, therefore, Theravance Biopharma will be entitled to injunctive relief with respect thereto in addition to any other remedies. The failure of either party to enforce its rights under this Agreement at any time for any period shall not be construed as a waiver of such rights.

12. Entire Agreement. This Agreement supersedes all prior agreements between the parties and constitutes the entire agreement between the parties as to the subject matter hereof, except that if the Consultant has signed a one-way nondisclosure agreement in favor of Theravance Biopharma or one of its affiliates, it shall remain in full force and effect.

13. Notices. All notices, requests and other communications called for by this Agreement shall be deemed to have been given if made in writing and mailed, postage prepaid, to the address of the party set forth above, or to such other addresses as the party shall specify to the others.

14. Amendments. No changes or modifications or waivers to this Agreement will be effective unless in writing and signed by both parties.

15. Severability. In the event that any provision of this Agreement shall be determined to be illegal or unenforceable, that provision will be limited or eliminated to the minimum extent necessary so that this Agreement shall otherwise remain in full force and effect and enforceable.

16. Counterparts and Facsimile and Electronic Signatures. This Agreement, and any subsequent amendment(s), may be executed in counterparts and the counterparts, together, will constitute a single agreement. A facsimile transmission or a Portable Document Format (PDF) sent by email of this signed Agreement bearing a signature on behalf of a party will be legal and binding on such party. In addition, (i) this Agreement may be executed and delivered via electronic mark, e-signature, or similar technology ("Electronic Signature"), and (ii) any Electronic Signature will constitute an original signature of a party, with the same binding effect as if executed and delivered in person by such party.

17. Arbitration. Subject to the exceptions set forth below, Consultant understands and agrees that any disagreement regarding this Agreement will be determined by submission to arbitration as provided by Section 1280 et seq. of the California Code of Civil Procedure, and not by a lawsuit or resort to court process proceedings. The only claims or disputes not covered by this paragraph are claims or disputes related to issues affecting the validity, infringement or enforceability of any trade secret or patent rights held or sought by Theravance Biopharma or which Theravance Biopharma could otherwise seek; in which case such claims or disputes shall not be subject to arbitration and will be resolved pursuant to applicable law.

18. Governing Law. This Agreement shall be governed by and construed in accordance with the laws of the State of California without regard to conflicts of law provisions thereof. In any action or proceeding to enforce rights under this Agreement, the prevailing party shall be entitled to recover costs and attorneys' fees.

19. Section 18 USC Notice. This Agreement does not affect any immunity under 18 USC Sections 1833(b) (1) or (2), which read as follows (note that for purposes of this statute only, individuals performing work as contractors or consultants are considered to be employees):

(1) An individual shall not be held criminally or civilly liable under any Federal or State trade secret law for the disclosure of a trade secret that (A) is made (i) in confidence to a Federal, State, or local government official, either directly or indirectly, or to an attorney; and (ii) solely for the purpose of reporting or investigating a suspected violation of law; or (B) is made in a complaint or other document filed in a lawsuit or other proceeding, if such filing is made under seal.

(2) An individual who files a lawsuit for retaliation by an employer for reporting a suspected violation of law may disclose the trade secret to the attorney of the individual and use the trade secret information in the court proceeding, if the individual (A) files any document containing the trade secret under seal; and (B) does not disclose the trade secret, except pursuant to court order.

Vijay Sabesan

/s/ Vijay Sabesan
(signature)

Date: November 30, 2021

Theravance Biopharma US, Inc.

By: /s/ Rick E Winningham
(signature)

Name: Rick E Winningham
Title: Chief Executive Officer

Date: November 30, 2021

EXHIBIT A

Description of Services

Consultant will perform the following Services at times that are mutually agreeable to both the Company and Consultant: due diligence and partnering support for certain programs, telephonic or electronic advice and consultation to the Company's Technical Operations and Business Development teams and related personnel concerning miscellaneous operational, partnering, data organization and/or transitional activities and/or assistance in other matters requiring institutional knowledge.

Consultant will be compensated as follows: on the next company vesting date (February 20, 2022), Consultant will vest in that portion of his currently outstanding restricted share units of Theravance Biopharma, Inc. that were otherwise expected to vest on November 20, 2022 in accordance with the terms of the agreements governing such awards.

Exhibit 10.71

EXECUTION COPY

SETTLEMENT AGREEMENT

THIS AGREEMENT is made **BETWEEN:**

THERAVANCE BIOPHARMA IRELAND LIMITED whose registered office is at Connaught House, 1 Burlington Road, Dublin 4, D04 C5Y6 (the "**Company**", which expression shall, where the context so permits or requires, include any Group Company (as defined below); and

ANN BRADY (the "**Employee**"),

together the "**Parties**" and each a "**Party**".

WHEREAS IT IS HEREBY AGREED IN CONSIDERATION OF THE PAYMENTS AND COVENANTS HEREINAFTER CONTAINED:

1. **BACKGROUND MATTERS**

1.1 The Employee's employment with the Company will terminate by reason of redundancy on 28 February 2022 (the "**Termination Date**").

1.2 The Parties have entered into this Agreement to record and implement the terms on which the Employee's employment is to terminate and on which they have agreed to settle any claims which the Employee has or may have in connection with their employment or its termination or otherwise against the Company, any Group and/or their current and former officers, agents, shareholders or employees, whether or not these claims are, or could be, in the contemplation of the Parties at the time of signing this Agreement and any updated waiver.

1.3 The Parties intend this Agreement to be an effective waiver of any such claims.

2. **TERMINATION AND RELATED MATTERS**

2.1 The Employee's employment with the Company will terminate on the Termination Date by reason of redundancy on the terms and subject to the conditions set out in this Agreement and without further obligation on the part of the Company, save as expressly provided for in this Agreement.

2.2 During the period from the date of this agreement up to the Termination Date, the Employee's existing responsibilities shall continue in accordance with her current terms of employment. In addition, the Employee shall conduct such additional duties as required to implement the strategic goals of the Company, including but not limited to:

(a) supporting the operational aspects of the proposed headcount reductions and restructuring of the business and the orderly disposition of certain partnerships (including by conducting redundancy consultations with impacted employees);

(b) liaising with the Company, other parts of the business and professional advisors as instructed by the Company;

(c) continuing to act in the best interest of the Company; and

(d) other specific duties as reasonably instructed from time to time.

2.3 The Employee shall be eligible to receive a discretionary bonus of €110,071.20 gross, subject to the successful achievement of agreed goals and strictly conditional on the Employee remaining in employment until the Termination Date. The achievement by the Employee of the agreed goals shall be at the sole discretion of the Company (which must be exercised reasonably).

2.4 On the Termination Date, the Employee shall sign an updated waiver in the terms of clause 3 of this Agreement.

2.5 Subject to strict compliance by the Employee with her obligations hereunder (and in particular clause 2.2), the Employee shall receive:

(a) a statutory redundancy payment in the amount of €7,620.00 gross;

(b) an ex gratia termination payment from the Company based on her service with the Company in the amount of €254,010.60 gross;

(c) an additional payment in the amount of €338,298.20 gross in recognition (and strictly conditional on) her performing the additional requirements set out at Paragraph 2 of these terms and strictly conditional on the Employee remaining in employment until the Termination Date;

(d) to the extent applicable, a gross lump sum payment in lieu of any accrued but untaken annual leave,

with the payments at 2.5(b) and 2.5(c) being referred to as the "**Termination Payments**".

2.6 The treatment of the Employee's outstanding equity awards to acquire ordinary shares of Theravance Biopharma, Inc. shall be governed by the applicable award agreement and plan rules, including but not limited to the Theravance Biopharma, Inc. 2013 Equity Incentive Plan (and the Irish Addendum thereto) or other applicable equity incentive plan. To the extent permissible under the rules of any applicable plans, subject to strict compliance by Employee with her obligations hereunder (and in particular Clause 2.2), the Employee's outstanding unvested restricted share unit awards (RU002373, RU002664, RU002776, RU002992 and RU003571) that would have vested over the next three fiscal quarters following the Termination Date (*i.e.*, May 20, 2022, August 20, 2022 and November 20, 2022) had she remained employed by the Company through such dates will benefit from accelerated vesting and vest on the Termination Date (the "**Vesting Acceleration"**). To the extent they vest, such restricted share units will be settled (*i.e.* the shares subject to such RSUs will be issued to the Employee) on a date or dates to be selected by the Company (expected to be during its open trading window in the second quarter 2022). The Employee acknowledges and agrees that vesting of her outstanding equity awards will cease on the Termination Date and that no further vesting will occur other than pursuant to this Clause 2.6 or pursuant to the Theravance Biopharma, Inc. Change in Control Severance Plan (the "**Severance Plan**").

2.7 To the extent Theravance Biopharma, Inc. is subject to a "Change in Control" (as defined in the Severance Plan) within three months after the Termination Date, Employee will be eligible for the severance benefits described in the Severance Plan on the terms and conditions set forth therein.

2.8 With effect from the Termination Date, the Company shall cease to be an active member of the Theravance Biopharma Ireland Limited Pension Scheme.

2.9 The Company agrees to make outplacement counselling available to the employee up to a maximum cost of €9,225 inclusive of VAT (the "**Outplacement Payment**"). Payment will be made by the Company directly to the outplacement agency upon receipt of a VAT invoice from the agency addressed to it.

2.10 All payments referred to at clause 2.3 and 2.5 above will be processed via payroll in the normal manner following the Termination Date.

2.11 The payments referred to at clause 2.3 and 2.5 are inclusive of any payments due to the Employee under statute, at common law or under the Employee's contract of employment. Save as expressly provided for in this Agreement, the Employee confirms that with effect from the Termination Date, they will have no entitlement to receive any additional payments of any kind from the Company or any Group Company in connection with their former employment by the Company and its termination (other than those due in respect of basic salary, pension contributions, car allowance and health insurance premium as set out in their contract of employment up to the Termination Date) whether in respect of remuneration, sick pay, annual leave, payment in lieu of annual leave, notice, payment in lieu of notice, health plan premium, car allowance commission, bonuses, benefits in kind or any other employment payments and/or benefits whatsoever.

2.12 All payments specified in this Agreement (and any payments in kind or benefits in kind) are subject to such tax and other deductions as the Company is required to deduct from the gross amount and remit to the Revenue Commissioners under the relevant tax and social welfare legislation.

2.13 In accordance with the Irish Addendum to the Theravance Biopharma, Inc. 2013 Equity Incentive Plan, Employee hereby appoints the Company as agent and/or attorney for the sale of such number of ordinary shares acquired by Employee pursuant to the vesting (whether as a result of the Vesting Acceleration or otherwise) and/or settlement of Employee's outstanding equity awards to cover: (i) any deductions that the Company and/or the Group Company is required by law to make, including but not limited to deduction of any income tax, universal social charge and employee pay related social insurance due as a result of such vesting and/or settlement; and (ii) all reasonable fees, commissions and expenses incurred in relation to such sale. Employee hereby authorise the payment to the Company and/or the Group Company of the appropriate amount out of the net proceeds of the sale of the ordinary shares.

2.14 The Company agrees to make the Termination Payments in an efficient manner permitted by law provided that the Company shall not be obliged to incur any additional cost, take any action which in its opinion is likely to be prejudicial to its commercial or reputational interests, incur additional risk or seek approval from any third party. The Employee shall, where requested to do so, provide the Company with information in a timely manner to allow it to assess the appropriate tax treatment of any termination payments. The Company has sole discretion as to the tax treatment to be applied to the payment and a delay in the provision in this information may result in a less efficient treatment of the Termination Payments.

2.15 The Employee hereby indemnifies the Company on demand against all and any liabilities to income tax, income levies, universal social charges, employee's pay related social insurance contributions or similar social security liabilities ("**Taxes**") and any interest or penalties thereon or costs related thereto which it may incur in respect of or by reason of payment of the Termination Payments, provided that they do not result from any unreasonable delay or default on the part of the Company and provided that if any demand is made of the Company in relation to the Taxes, the Company will

as soon as reasonably practicable upon receipt of any request for payment, assessment, demand or other notification of liability or potential liability to Taxes, or it otherwise becoming aware of any circumstances which may give rise to a claim under this indemnity, inform the Employee and give the Employee an opportunity to comment on any such demand and to make representations to promptly resolve the matter directly to Revenue.

3. **RELEASE AND DISCHARGE**

3.1 The terms of this Agreement have been offered by the Company and are accepted by the Employee strictly without admission of liability on the part of the Company.

3.2 The Employee acknowledges and agrees that the provisions of this Agreement, and in particular, the Termination Payments, the Vesting Acceleration and the Outplacement Payment constitute a full and final settlement of any claims, rights of action and demands made and/or which may be made in any jurisdiction by the Employee against the Group and/or any of their respective current and former officers, directors, members or employees and/or professional service providers in connection with their employment by the Company or the termination of such employment, whether such claims arise at common law, in equity, in tort, in contract or pursuant to statute (including but not limited to the Workplace Relations Act 2015 (as amended or extended from time to time), the Redundancy Payments Acts 1967 to 2014, Minimum Notice and Terms of Employment Acts 1973 to 2005, Payment of Wages Act 1991, Organisation of Working Time Act 1997, Employment Equality Acts 1998 to 2015, the Terms of Employment (Information) Acts 1994 to 2014, the Protection of Employment Acts 1977 to 2014, the Data Protection Acts 1988 to 2018, the Protection of Employees (Part-time Work) Act 2001, the Protection of Employees (Fixed-Term Work) Act 2003, the Industrial Relations Acts 1946 to 2015, the Pensions Acts 1990 to 2015, the Maternity Protection Acts 1994 to 2004, the Paternity Leave and Benefit Act 2016, the Adoptive Leave Acts 1995 to 2005, the Parental Leave Acts 1998 to 2019, the Carers Leave Act, 2001, the National Minimum Wage Acts, 2000 to 2015, the European Communities (Protection of Employees on Transfer of Undertakings) Regulations 2003, the Safety, Health and Welfare at Work Acts 2005 to 2014, the Protected Disclosures Act 2014 and the Unfair Dismissals Acts 1977 to 2015 as amended) and/or pursuant to other employee protection legislation or for personal injury or otherwise howsoever arising whether such claims are or could be known to the Parties or in the contemplation of the Parties at the date of this Agreement.

4. **DIRECTORSHIPS**

4.1 The Employee shall continue to serve as a director of the Company up to the Termination Date, unless requested before that date to resign that directorship by the Company, the Board of the Company or any other party authorised by the Board of the Company. On receipt of a request to resign that directorship the Employee shall immediately provide the Company with a signed resignation letter in substantially the same format the agreed form letter at Appendix I hereto. If the Employee refuses to provide such a signed resignation letter the Employee hereby irrevocably appoints Brett A. Grimaud to be the Employee's attorney and/or agent and in the Employee's name and on the employee's behalf to do all such acts and things and to sign all resignation letters and documents as may be necessary to effect the Employee's resignation from office with the Company.

5. **RETURN OF COMPANY PROPERTY**

Save as expressly provided for in this Agreement, the Employee warrants that they will, on or before the Termination Date, return to the Company in good condition any and all property belonging to or relating to the business of the Company and any Group Company which is in the Employee's possession, custody or control, including, without limitation access swipe cards, the Company's computer equipment and all other IT equipment and devices, all computer records relating to the Company or to the customers or suppliers of the Company, all printers, laptops, fax machines, mobile phones, corporate credit and security cards, all Company records and all other data and documentation in the Employee's possession or under the Employee's control pertaining to the business and affairs of the Company and all other Company property in the Employee's possession or under the Employee's control.

6. **EMPLOYEE WARRANTY**

The Employee also warrants that up to and as at the date of this Agreement the Employee:

6.1 has not committed any breach of any duty owed to the Company (and for the avoidance of doubt has not admitted the Company to any contractual obligation with any third party of which the Company is not already aware);

6.2 has not, done or failed to do anything which amounts to a repudiatory breach of the express or implied terms of the employment with the employer or which, if it had been done or omitted after the execution of this Agreement, would have been in breach of any of its terms;

6.3 is not aware of any matters relating to any acts or omissions by the Employee or by any director, officer, employee or agent of the Company which if disclosed to the Company might affect its decision to enter into this Agreement; and

6.4 that if the Employee issues or commences any claims or proceedings against the Company, any Group Company and/or any of their current and former officers, directors, employees or agents in relation to claims accepted as settled pursuant to clause 3, the Employee agrees to repay to the Company on demand a sum equal to the value after deduction of income tax and social/national insurance contributions of the Termination Payments. The Employee agrees that in such circumstances the said sum shall be recoverable from the Employee by the Company as debt.

7. **NON-DISCLOSURE**

Both Parties agree to keep the fact of and terms of this Agreement strictly private and confidential and agree not to disclose the same to any third party save where such disclosure is required by the law of any jurisdiction (including, for the avoidance of doubt, securities laws).

8. **CONFIDENTIALITY**

8.1 The Employee acknowledges that during the term of the employment, the Employee had access to confidential information that is confidential and proprietary to the Company, including but not limited to trade secrets, technical data, information of a business, financial or technical nature and other confidential information relating to the business and affairs of the Company. The Employee undertakes and agrees that all such confidential information shall be and remain at all times the exclusive property of the Company. The Employee further undertakes and agrees that they will not at any time disclose such confidential information to anyone else or utilise it for their own benefit or for the benefit of others without the prior written consent of a duly authorised officer of the Company.

8.2 The Employee agrees that they shall continue to be bound by the confidentiality provisions contained within their terms and conditions of employment as well as her common law duties of fidelity and confidentiality.

8.3 In the event that the Employee breaches the confidentiality obligations set out in their contract of employment, at common law or this Agreement, the Company fully reserves its rights in relation to any action it may take arising from same. For the avoidance of doubt, this may include but not be limited to the withholding of certain of the payments and benefits set out in this Agreement.

9. CONFIRMATION OF INDEPENDENT LEGAL ADVICE

9.1 The Employee warrants that they have had the opportunity to take independent legal advice on the terms and effect of this Agreement and that the Company has confirmed that its willingness to offer a contribution of €1,000 exclusive of VAT towards the Employee's legal costs in reviewing this Agreement. Payment will be made by the Company directly to the employee's solicitor upon receipt of a VAT invoice from the agency addressed to the employee but marked payable by the Company.

9.2 The Employee hereby acknowledges that they understand and accept the effect and implications of this Agreement and that they are entering into this Agreement without coercion of any description and with full understanding that they are releasing and compromising any and all claims that they have or may have against the Group and each of their current and former officers, directors, members or employees and/or professional service providers arising from and/or connected with her former employment with the Company and/or the termination of such employment.

10. GENERAL

10.1 This Agreement shall be binding on the Parties on signature by both the Employee and on behalf of the Company.

10.2 Save as expressly provided herein, this Agreement supersedes all previous agreements and arrangements (oral or in writing) in relation to any of the matters dealt with within it, and represents the entire agreement reached between the Parties.

10.3 The Parties warrant, represent and undertake to adhere to the terms of this Agreement.

11. COUNTERPARTS

This Agreement may be signed in any number of counterparts, each of which, when signed, shall be an original and all of which together evidence the same agreement.

12. GOVERNING LAW AND JURISDICTION

This Agreement is governed by and shall be construed in accordance with the laws of Ireland and the courts of Ireland will have exclusive jurisdiction in relation to any disputes arising in relation to it. Any proceedings, suit or action arising out of or in connection with this Agreement shall therefore be brought in the courts of Ireland.

13. SUBJECT TO CONTRACT AND WITHOUT PREJUDICE

This Agreement shall be without prejudice and subject to contract until such time as it is signed by both Parties, when it shall be treated as an open document evidencing a binding agreement.

14. DEFINITION

The definitions in this clause apply in this Agreement.

Group: the Company and any Group Company; and

Group Company: any undertaking which for the time being is a subsidiary undertaking or joint venture of the Company, a holding undertaking of which the Company is a subsidiary undertaking, or a subsidiary undertaking or joint venture of such holding undertaking, or an undertaking in which any of the foregoing has a participating interest (the terms "undertaking", "subsidiary undertaking" and "holding undertaking" each having the meaning given to it in section 275 of the Companies Act 2014, and the terms "joint venture" and "participating interest" each having the meaning given to it in Schedule 4A to that Act).

Appendix I
Agreed Form Letter of Resignation of Directorship(s)

The Directors
Theravance Biopharma Ireland Limited

Re: Resignation from office.
Theravance Biopharma Ireland Limited (the 'Company')

Dear Sirs and Madams,

Take Notice that with effect from the date hereof I hereby resign as a director of the Company and I acknowledge I have no claim for compensation for loss of office, loss of fees, breach of contract, termination of employment or on any other account whatsoever. I confirm that as of the date hereof I have no claims against the Company or any of its holding companies, associated companies or subsidiaries or current or former shareholders, officers or employees whether in Ireland or any other jurisdiction and whether such claims arise in contract, equity, tort, at common law, pursuant to statute or otherwise. I confirm that all fees and expenses due to me have been discharged up to date

Yours faithfully

_____

Ann Brady

Dated:

IN WITNESS whereof the Parties have executed this Agreement in the manner hereinafter appearing:

SIGNED by **THERAVANCE BIOPHARMA, INC.** for and on behalf of
THERAVANCE BIOPHARA IRELAND LIMITED

/s/ Rick E Winningham

Rick E Winningham

Dated the 2nd day of November, 2021

/s/ Ann Brady

SIGNED by **ANN BRADY**

in the presence of: /s/ witness

Dated the 2nd day of November, 2021

Theravance Respiratory Company, LLC

Financial Statements as of and for the Three Years Ended
December 31, 2021
and Report of Independent Registered Public Accounting Firm

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Members and the Board of Directors of Theravance Respiratory Company, LLC

Opinion on the Financial Statements

We have audited the accompanying balance sheet of Theravance Respiratory Company, LLC (a Delaware limited liability company) (the "Company") as of December 31, 2021, the related statements of income and comprehensive income, changes in members' equity, and cash flows for the year ended December 31, 2021, and the related notes (collectively referred to as the "financial statements"). In our opinion, the financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2021, and the results of its operations and its cash flows for the year ended December 31, 2021, in conformity with accounting principles generally accepted in the United States of America.

Basis for Opinion

These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's financial statements based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) ("PCAOB") and are required to be independent with respect to the Company in accordance with U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audit in accordance with the standards of the PCAOB and in accordance with auditing standards generally accepted in the United States of America. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audit we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion.

Our audit included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audit also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audit provides a reasonable basis for our opinion.

Critical Audit Matter

The critical audit matter communicated below is a matter arising from the current period audit of the financial statements that was communicated or required to be communicated to the audit committee and that: (1) relates to accounts or disclosures that are material to the financial statements and (2) involved our especially challenging, subjective, or complex judgments. The communication of critical audit matters does not alter in any way our opinion on the financial statements, taken as a whole, and we are not, by communicating the critical audit matter below, providing a separate opinion on the critical audit matters or on the accounts or disclosures to which it relates.

Consolidation of Investees

As described further in Note 3 to the financial statements, certain of the Company's investments have complex structures and agreements which must be evaluated for consolidation, including determining whether the investee is a variable interest entity ("VIE"), and if so, whether the Company is the primary beneficiary. This assessment is performed at the inception of the investment and upon the occurrence of reconsideration events and requires significant judgment by management.

As of December 31, 2021, the Company did not have any consolidated VIEs. As of December 31, 2021, the Company's investments in unconsolidated VIEs was $37.7 million.

We identified the assessment of consolidation of investees as a critical audit matter. The principal consideration for our determination that the consolidation determination for the Company's investees either at inception or upon a reconsideration event is a critical audit matter is that there is significant judgment required by management to interpret complex structures and agreements. This required a high degree of auditor judgment and an increased audit effort.

Our audit procedures related to consolidation and primary beneficiary assessment included the following, among others.

- We evaluated the design effectiveness of controls related to management's initial accounting assessment for each investment.
- We evaluated the Company's accounting analysis for all significant investees by performing procedures including, but not limited to:
  - Obtaining an understanding of the composition and governance of the investee, its board of directors and management.
  - Reading the purchase agreements and other related documents and evaluating the structures and terms of the agreements to verify if the investments should be classified as VIEs.
  - If an investee is determined to be a VIE, considering whether the Company appropriately determined the primary beneficiary by evaluating the investment arrangements of the entity to determine if the Company has the power to direct activities, and if the Company has the obligation to absorb losses of the entity or the right to receive benefits from the entity that could be significant to the VIE.
  - Evaluating the evidence obtained in other areas of the audit to determine if there were additional reconsideration events that had not been identified by the Company, including reading board minutes and confirming the terms of certain agreements, as applicable.

/s/ GRANT THORNTON LLP

We have served as the Company's auditor since 2021.

San Francisco, California
February 25, 2022

THERAVANCE RESPIRATORY COMPANY, LLC
BALANCE SHEETS
(In thousands)

	December 31, 2021	December 31, 2020 (unaudited)
Assets		
Current assets:		
Cash and cash equivalents	$ 50,713	$ 38,081
Related party receivables from collaborative arrangements	42,492	24,946
Prepaid expenses and other current assets	71	—
Total current assets	93,276	63,027
Equity and long-term investments	37,695	16,959
Total assets	$ 130,971	$ 79,986
Liabilities and Equity		
Current liabilities:		
Accrued liabilities	252	508
Total current liabilities	252	508
Equity:		
Capital contributions (distributions), net	(125,196)	(55,246)
Retained earnings	255,915	134,724
Total equity	130,719	79,478
Total liabilities and equity	$ 130,971	$ 79,986

See accompanying notes to financial statements.

THERAVANCE RESPIRATORY COMPANY, LLC
STATEMENTS OF INCOME AND COMPREHENSIVE INCOME
(In thousands)

	Year Ended December 31,		
	2021	2020 (unaudited)	2019 (unaudited)
Revenue:			
Royalty revenue from a related party	$ 126,688	$ 73,090	$ 42,790
Revenue from collaborative arrangements with a related party	—	10,000	—
Total revenue	126,688	83,090	42,790
Operating expenses:			
General and administrative	3,956	2,613	3,381
Total operating expenses	3,956	2,613	3,381
Income from operations	122,732	80,477	39,409
Interest income	—	38	244
Changes in fair values of equity and long-term investments, net	(1,541)	1,147	—
Net income	$ 121,191	$ 81,662	$ 39,653
Comprehensive income	$ 121,191	$ 81,662	$ 39,653

See accompanying notes to financial statements.

THERAVANCE RESPIRATORY COMPANY, LLC
STATEMENTS OF CHANGES IN MEMBERS' EQUITY
(In thousands)

	Innoviva (1)	Theravance Biopharma (2)	Total Equity
Balance as of January 1, 2019 (unaudited)	$ 965	$ 5,465	$ 6,430
Distributions	(1,862)	(10,553)	(12,415)
Net income	5,948	33,705	39,653
Balance as of December 31, 2019 (unaudited)	$ 5,051	$ 28,617	$ 33,668
Distributions	(5,378)	(30,474)	(35,852)
Net income	12,249	69,413	81,662
Balance as of December 31, 2020 (unaudited)	$ 11,922	$ 67,556	$ 79,478
Distributions	(10,493)	(59,457)	(69,950)
Net income	18,179	103,012	121,191
Balance as of December 31, 2021	$ 19,608	$ 111,111	$ 130,719

(1) Innoviva Inc. and its subsidiary ("Innoviva" collectively) own a 15% economic interest.
(2) Theravance Biopharma Inc. and its subsidiaries ("Theravance Biopharma" collectively) own the remaining 85% of the economic interests.

See accompanying notes to financial statements.

THERAVANCE RESPIRATORY COMPANY, LLC
STATEMENTS OF CASH FLOWS
(In thousands)

	Year Ended December 31,		
	2021	2020	2019
		(unaudited)	(unaudited)
Cash flows from operating activities			
Net income	$ 121,191	$ 81,662	$ 39,653
Adjustments to reconcile net income to net cash provided by operating activities:			
Changes in fair values of equity and long-term investments, net	1,541	(1,147)	—
Changes in operating assets and liabilities:			
Receivables from collaborative arrangements	(17,546)	(10,558)	(7,955)
Prepaid expenses and other current assets	(71)	10	(10)
Accrued liabilities	(256)	(2,561)	3,066
Net cash provided by operating activities	104,859	67,406	34,754
Cash flows from investing activities			
Purchases of equity and long-term investments	(22,277)	(15,812)	—
Net cash used in investing activities	(22,277)	(15,812)	—
Cash flows from financing activities			
Distributions	(69,950)	(35,852)	(12,415)
Net cash used in financing activities	(69,950)	(35,852)	(12,415)
Net increase (decrease) in cash and cash equivalents	12,632	15,742	22,339
Cash and cash equivalents at beginning of period	38,081	22,339	—
Cash and cash equivalents at end of period	$ 50,713	$ 38,081	$ 22,339

See accompanying notes to financial statements.

1. Description of Operations and Summary of Significant Accounting Policies

Description of Operations

Theravance Respiratory Company, LLC (referred to as "TRC", the "Company", or "we" and other similar pronouns) is a company with a portfolio of royalties and other healthcare assets. Our royalty portfolio primarily contains a respiratory asset, TRELEGY® ELLIPTA® (the combination FF/UMEC/VI), partnered with Glaxo Group Limited ("GSK"). The Company was set up as a limited liability company in the state of Delaware in 2014. It is owned by Innoviva Inc. and its subsidiary ("Innoviva" collectively) with a 15% economic interest and Theravance Biopharma Inc. and its subsidiaries ("Theravance Biopharma" collectively) with the remaining 85% of the economic interests. Innoviva is the managing member of TRC.

Use of Management's Estimates

The preparation of financial statements in conformity with U.S. Generally Accepted Accounting Principles ("GAAP") requires management to make estimates and assumptions that affect the amounts reported in the financial statements and accompanying notes. Actual results could differ materially from those estimates. Management evaluates its significant accounting policies and estimates on an ongoing basis. We base our estimates on historical experience and other relevant assumptions that we believe to be reasonable under the circumstances. These estimates also form the basis for making judgments about the carrying values of assets and liabilities when these values are not readily apparent from other sources.

Certain Risks and Concentrations

Our financial instruments that are exposed to concentrations of credit risk consist primarily of cash and cash equivalents, marketable securities, and equity and long-term investments. Although we deposit our cash with a financial institution, our deposits, at times, may exceed federally insured limits. Refer to "Segment Reporting" below for concentrations with respect to revenues and geographic locations.

Segment Reporting

We operate in a single segment, which is to provide capital return to the Company's owners by maximizing the potential value of our respiratory asset partnered with GSK. Revenues are generated from our collaborative arrangements and royalty payments from GSK, located in Great Britain. Our facilities are located within the United States.

Variable Interest Entities

We evaluate our ownership, contractual and other interest in entities to determine if they are variable interest entities ("VIE"). We evaluate whether we have a variable interest in those entities and the nature and extent of those interests. Based on our evaluation, if we determine we are the primary beneficiary of a VIE, we consolidate the entity in our financial statements.

Cash and Cash Equivalents

We consider all highly liquid investments purchased with a maturity of three months or less on the date of purchase to be cash equivalents. Cash equivalents are carried at cost, which approximates fair value.

Equity and Long-Term Investments

We invest from time to time in equity and debt securities of private companies. If we determine that we have control over these companies under either voting or VIE models, we consolidate them in our financial statements. If we determine that we do not have control over these companies under either voting or VIE models, we then determine if we have an ability to exercise significant influence via voting interests, board representation or other business relationships.

We may account for the investments where we exercise significant influence using either an equity method of accounting or at fair value by electing the fair value option under Accounting Standards Codification ("ASC") Topic 825, *Financial Instruments*. If the fair value option is applied to an investment that would otherwise be accounted for under the equity method, we apply it to all our financial interests in the same entity (equity and debt, including guarantees) that are eligible items. All gains and losses from fair value changes, unrealized and realized, are presented as changes in fair values of equity and long-term investments, net on the statements of income.

If we conclude that we do not have an ability to exercise significant influence over an investee, we may elect to account for the security without a readily determinable fair value using the measurement alternative under ASC Topic 321, *Investments – Equity Securities*. This measurement alternative allows us to measure the equity investment at its cost minus impairment, if any, plus or minus changes resulting from observable price changes in orderly transactions for the identical or a similar investment of the same issuer.

Fair Value of Financial Instruments

We define fair value as the exchange price that would be received for an asset or paid to transfer a liability (an exit price) in the principal or most advantageous market for the asset or liability in an orderly transaction between market participants on the measurement date.

Our valuation techniques are based on observable and unobservable inputs. Observable inputs reflect readily obtainable data from independent sources, while unobservable inputs reflect our market assumptions. We classify these inputs into the following hierarchy:

Level 1—Quoted prices for identical instruments in active markets.

Level 2—Quoted prices for similar instruments in active markets; quoted prices for identical or similar instruments in markets that are not active; and model-derived valuations whose inputs are observable or whose significant value drivers are observable.

Level 3—Unobservable inputs and little, if any, market activity for the assets.

Financial instruments include cash equivalents, receivables from collaborative arrangements, prepaid expenses and other current assets, and accrued liabilities. Cash equivalents are carried at estimated fair value. The carrying values of receivables from collaborative arrangements and accrued liabilities approximate their estimated fair values due to the relatively short-term nature of these instruments.

Revenue Recognition

Revenue is recognized when our customer obtains control of promised goods or services, in an amount that reflects the consideration which we expect to receive in exchange for those goods or services. Revenue is recognized through a five-step process: (i) identify the contract with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price for the contract; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue as a performance obligation is satisfied.

We recognize the royalty revenue on net sales of products with respect to which we have contractual royalty rights in the period in which the royalties are earned. The net sales reports provided by our partner are based on its methodology and assumptions to estimate rebates and returns, which it monitors and adjusts regularly in light of contractual and legal obligations, historical trends, past experience and projected market conditions. Our partner may make significant adjustments to its sales based on actual results recorded, which could cause our royalty revenue to fluctuate. We have the ability to conduct periodic royalty audits to evaluate the information provided by our partner.

Related Parties

While GSK no longer had an ownership stake in Innoviva as of December 31, 2021, it remains as Theravance Biopharma's major stockholder. GSK is considered a related party due to our collaborative arrangement with them. Transactions with GSK are described in Note 2, "Revenue Recognition and Collaborative Arrangements."

Innoviva provides management and administrative services and support at no charge to the Company. If these amounts were charged, the reported results could be materially different.

2. Revenue Recognition and Collaborative Arrangements

We recognize royalty revenue on net sales of TRELEGY® ELLIPTA® with respect to which we have contractual royalty rights in the period in which the royalties are earned.

LABA Collaboration

In November 2002, Innoviva entered into the LABA Collaboration Agreement with GSK to develop and commercialize once-daily LABA products for the treatment of chronic obstructive pulmonary disease ("COPD") and asthma. In connection with the spin-off of Innoviva's research and development operations to Theravance Biopharma, Inc. in 2014, the agreement was assigned to TRC for TRELEGY® ELLIPTA®. Manufacturing and commercialization of TRELEGY® ELLIPTA® are performed by GSK. TRC is entitled to receive royalties from GSK on sales of TRELEGY® ELLIPTA®. Royalties are upward tiering and range from 6.5% to 10%. Royalty revenues for the year ended December 31, 2021, 2020 and 2019 were $126.7 million, $73.1 million (unaudited), and $42.8 million (unaudited), respectively.

2004 Strategic Alliance

In March 2004, Innoviva entered into the Strategic Alliance Agreement with GSK where GSK received an option to license exclusive development and commercialization rights to product candidates from certain of Innoviva's discovery programs on predetermined terms and on an exclusive, worldwide basis. In 2005, GSK licensed Innoviva's Bifunctional Muscarinic Antagonist-Beta2 Agonist ("MABA") program for the treatment of COPD. The development program was funded by GSK. In 2014, the agreement was assigned to TRC in connection of the spin-off. In 2020, GSK terminated the MABA program and paid us a $10.0 million (unaudited) termination fee.

3. Financial Instruments and Fair Value Measurements

Equity Investment in InCarda

During the third quarter of 2020, TRC purchased 20,469,432 shares of Series C preferred stock and warrants to purchase 5,117,358 additional shares of Series C preferred stock of InCarda Therapeutics, Inc. ("InCarda") for $15.8 million (unaudited), which includes $0.8 million (unaudited) of transaction costs. InCarda is a privately held biopharmaceutical company focused on developing inhaled therapies for cardiovascular diseases. The investment is intended to fund the ongoing clinical development of InRhythm™ (flecainide for inhalation), the company's lead program, for the treatment of a recent-onset episode of paroxysmal atrial fibrillation. TRC has the right to designate one member to InCarda's board. As of December 31, 2021, one of InCarda's eight board members is designated by TRC. As of December 31, 2021 and 2020, TRC held 13.0% and 13.4% (unaudited) of InCarda equity ownership.

The investment in InCarda does not provide TRC the ability to control or have significant influence over InCarda's operations. Based on our evaluation, we determined that InCarda is a VIE, but TRC is not the primary beneficiary of the VIE. We have accounted for the investment in Series C preferred shares in InCarda using the measurement alternative because the securities are not publicly traded and do not have a readily determinable fair value. Under the measurement alternative, the equity investment is initially recorded at its allocated cost, but the carrying value may be adjusted through earnings upon an impairment or when there is an observable price change involving the same or a similar investment with the same issuer. As of December 31, 2021 and 2020, we recorded $15.8 million for our investment in InCarda's series C preferred stock as equity and long-term investments on the balance sheets. There was no impairment or other change to the value of the InCarda's Series C preferred stock as of December 31, 2021 and 2020, respectively.

The warrants are recorded at fair value and subject to remeasurement at each balance sheet date. The warrants are exercisable immediately with an exercise price of $0.7328 per share. In September 2021, TRC and InCarda entered into an amendment to extend the expiration date of the warrants from October 6, 2021 to March 31, 2022. We use the Black-Scholes-Merton pricing model to estimate the fair value of the warrants with the following input assumptions: the exercise price of the warrants, the risk-free interest rate computed based on the U.S. Treasury yield, the remaining contractual term as the expected term, and the expected stock price volatility calculated based on the historical volatility of the common stock of its public peer companies.

As of December 31, 2021 and 2020, the fair value of InCarda's warrants was estimated at $0.4 million and $1.1 million (unaudited), respectively, and recorded as equity and long-term investments on the balance sheets. We recorded $0.7 million unrealized loss and $1.1 million (unaudited) unrealized gains as changes in fair values of equity and long-term investments, net on the statements of income for the years ended December 31, 2021 and 2020, respectively.

Equity Investment in ImaginAb

On March 18, 2021, TRC entered into a securities purchase agreement with ImaginAb, Inc. (“ImaginAb”) to purchase 4,051,724 shares of ImaginAb Series C preferred stock for $4.7 million. On the same day, TRC also entered into a securities purchase agreement with one of ImaginAb’s common stockholders to purchase 4,097,157 shares of ImaginAb common stock for $1.3 million. ImaginAb is a privately held biotechnology company focused on clinically managing cancer and autoimmune diseases via molecular imaging. $0.4 million was incurred for investment due diligence costs and execution and recorded as part of the equity and long-term investment on the balance sheet. As of December 31, 2021, one of ImaginAb’s five board members is designated by TRC, and TRC held 14.5% of ImaginAb’s equity.

The investment in ImaginAb does not provide TRC the ability to control or have significant influence over ImaginAb's operations. Based on our evaluation, we determined that ImaginAb is a VIE, but TRC is not the primary beneficiary of the VIE. Because ImaginAb’s equity securities are not publicly traded and do not have a readily determinable fair value, we have accounted for our investment in ImaginAb’s Series C preferred stock and common stock using the measurement alternative. Under the measurement alternative, the equity investment is initially recorded as its allocated cost, but the carrying value may be adjusted through earnings upon an impairment or when there is an observable price change involving the same or a similar investment with the same issuer. As of December 31, 2021, $6.4 million was recorded as equity and long-term investments on the balance sheet and there was no change to the fair value of our investment.

Convertible Promissory Note in Gate Neurosciences

On November 24, 2021, TRC entered into a Convertible Promissory Note Purchase Agreement with Gate Neurosciences, Inc. (“Gate”) to acquire a convertible promissory note (the “Convertible Note”) with a principal amount of $15.0 million. Gate is a privately held biopharmaceutical company focused on developing the next generation of targeted nervous system therapies, leveraging precision medicine approaches to develop breakthrough drugs for psychiatric and neurologic diseases. The investment is intended to fund its ongoing development and research. The Convertible Note bears an annual interest rate of 8% and will convert into common stock shares upon a qualified event or into shares of shadow preferred stock (“Shadow Preferred”) upon a qualified financing. A qualifying event can be a qualified initial price offering, a qualified merger, or a merger with a special-purpose acquisition company (“SPAC”).

The number of common stock shares to be issued in a qualified event shall be equal to the amount due on the conversion date divided by the lesser of a capped conversion price (the "Capped Conversion Price") and the qualified event price (the "Qualified Event Price"). The Capped Conversion Price is calculated as $50.0 million divided by the number of common stock outstanding at such time on a fully diluted basis. The Qualified Event Price is the price per share determined by the qualified event. A qualified financing is a sale or series of sales of preferred stock where (i) at least 50 percent of counterparties are not existing shareholders, (ii) net proceeds to Gate are at least $35.0 million, and (iii) the stated or implied equity valuation of Gate is at least $80.0 million. Shadow Preferred means preferred stock having identical rights, preferences and restrictions as the preferred stock that would be issued in a qualified financing.

The investment in Gate does not provide TRC the ability to control or have significant influence over Gate's operations. Based on our evaluation, we determined that Gate is a VIE, but TRC is not the primary beneficiary of the VIE. We have accounted for the convertible debt investment as a trading security, measured at fair value using a Monte Carlo simulation model with the probability of certain qualified events. TRC has the right to designate one board member to Gate's board. As of December 31, 2021, TRC has not designated a board member to Gate’s board, which currently consists of two directors. As of December 31, 2021, $15.9 million, which includes $0.9 million of transaction costs, was recorded as equity and long-term investments on the balance sheet before unrealized losses. We recorded $0.8 million unrealized loss as changes in fair values of equity and long-term investments, net on the statement of income for the year ended December 31, 2021.

Fair Value Measurements

Certain of our equity and long-term investments are measured at fair value on a recurring basis. The estimated fair values were as follows:

	Estimated Fair Value Measurements as of December 31, 2021 Using:			
Types of Instruments (In thousands)	**Quoted Price in Active Markets for Identical Assets Level 1**	**Significant Other Observable Inputs Level 2**	**Significant Unobservable Inputs Level 3**	**Total**
Assets				
Equity investment - InCarda Warrants	—	—	411	411
Convertible debt investment - Gate Note	—	—	15,100	15,100
Total assets measured at estimated fair value	$ —	$ —	$ 15,511	$ 15,511

	Estimated Fair Value Measurements as of December 31, 2021 Using: (unaudited)			
Types of Instruments (In thousands)	**Quoted Price in Active Markets for Identical Assets Level 1**	**Significant Other Observable Inputs Level 2**	**Significant Unobservable Inputs Level 3**	**Total**
Assets				
Equity investment - InCarda Warrants	—	—	1,147	1,147
Total assets measured at estimated fair value	$ —	$ —	$ 1,147	$ 1,147

InCarda's warrants and Gate's convertible note are classified as Level 3 financial instruments as these securities are not publicly traded and the assumptions used in the valuation model for valuing these securities are based on significant unobservable and observable inputs including those of publicly traded peer companies.

4. General and Administrative Expenses

The majority of the general and administrative expenses was legal expenses. For the year ended December 31, 2021, 2020 and 2019, legal fees incurred for the arbitrations between TRC, Innoviva and Theravance Biopharma were $3.3 million, $1.7 million (unaudited) and $3.0 million (unaudited), respectively.

In May 2019, Theravance Biopharma initiated arbitration against Innoviva and TRC, relating to a dispute as to the determination by Innoviva (as manager of TRC) to cause TRC to explore potential reinvestment opportunities for the royalty proceeds received by GSK into initiatives that Innoviva believes will increase the value of TRC and TRELEGY® ELLIPTA®. Theravance Biopharma alleged that, in causing TRC to not distribute substantially all royalty proceeds received from GSK, Innoviva breached the limited liability company operating agreement governing TRC (the "Operating Agreement"), as well as the fiduciary duties applicable to Innoviva as manager of TRC. The hearing in respect of the arbitration was conducted from July 23, 2019 through July 25, 2019. Post-arbitration oral argument was heard on August 14, 2019. On September 26, 2019, the arbitrator issued a final decision. The arbitrator ruled that Innoviva did not breach the Operating Agreement or its fiduciary duties by withholding royalties or pursuing reinvestment opportunities. Accordingly, the Company is permitted to continue to pursue development and commercialization initiatives. The arbitrator did conclude that Innoviva breached a provision of the Operating Agreement requiring Innoviva to deliver quarterly financial plans to Theravance Biopharma. However, the arbitrator concluded that this technical breach did not cause any damages to Theravance Biopharma and the arbitrator awarded limited injunctive relief to expand and clarify the disclosure obligations under the Operating Agreement related to the delivery of financial plans and the pursuit of investment opportunities (if those opportunities related to TRELEGY® ELLIPTA®). Finally, the arbitrator ruled that Innoviva was entitled to indemnification from TRC for 95% of its fees and expenses incurred in connection with the arbitration.

On September 30, 2019, Innoviva and TRC filed a Verified Complaint in the Court of Chancery of the State of Delaware ("Court of Chancery") to confirm the arbitration award. The award was confirmed by the Court of Chancery on May 4, 2020.

On July 16, 2020, Innoviva and TRC initiated a lawsuit in the Court of Chancery against Theravance Biopharma, seeking a permanent injunction preventing Theravance Biopharma from interfering with Innoviva's ability to cause TRC to reserve cash to pursue non-Trelegy related investment opportunities and a declaration that the arbitration award conclusively established that Innoviva, as manager of TRC, has such authority. The Court of Chancery directed the parties to obtain the arbitrator's opinion as to

whether the arbitration award addressed non-Trelegy related investment opportunities. On July 31, 2020, the arbitrator, while reiterating that Innoviva has broad authority as manager of TRC, found that his award did not specifically address this situation. Accordingly, on August 5, 2020, the parties stipulated to the dismissal of the Court of Chancery action.

On October 6, 2020, Theravance Biopharma initiated a new arbitration against Innoviva and TRC, challenging Innoviva's authority as manager of TRC to cause TRC to pursue non-Trelegy related investment opportunities and again alleging that Innoviva is required to cause TRC to distribute substantially all royalty proceeds from GSK. The hearing in respect of the arbitration was conducted from February 16, 2021 through February 19, 2021. Post-arbitration oral argument was heard on March 8, 2021. On March 30, 2021, the arbitrator issued a final decision. The arbitrator ruled that Innoviva did not breach the Operating Agreement or its fiduciary duties by withholding royalties to pursue non-Trelegy-related investment opportunities. Additionally, the arbitrator ruled that Innoviva is entitled to indemnification from TRC for 100% of its fees and expenses reasonably incurred in connection with the arbitration.

On April 15, 2021, Innoviva and TRC filed a Verified Complaint in the Court of Chancery to confirm the arbitration award. On May 19, 2021, Theravance Biopharma submitted an answer to the Verified Complaint and filed a Motion to Modify the Arbitral Award, alleging that it contained a mathematical error. The parties filed a proposed stipulation to remand the motion to Chancellor Chandler for his consideration, which the Court of Chancery granted. On June 25, 2021, Innoviva submitted a brief to Chancellor Chandler in opposition to the motion and on July 15, 2021, Theravance Biopharma submitted a reply brief. On August 6, 2021, Chancellor Chandler issued a modified final award, which did not affect any of his ultimate conclusions. The modified award was confirmed by the Court of Chancery on September 16, 2021.

5. Commitments and Contingencies

We indemnify our members for certain events or occurrences, subject to certain limits. We may be subject to contingencies that may arise from matters such as product liability claims, legal proceedings, shareholder suits and tax matters. As such, we are unable to estimate the potential exposure related to these indemnification agreements. We have not recognized any liabilities relating to these agreements as of December 31, 2021.

6. Subsequent Events

On February 18, 2022, TRC entered into an investment and shareholders agreement with Nanolive SA ("Nanolive") to purchase 18,750,000 shares of Series C preferred stock for $9.8 million (equivalent to 9.0 million CHF). Nanolive SA is a Swiss privately held life sciences company focused on developing breakthrough imaging solutions that accelerate research in growth industries such as drug discovery and cell therapy. TRC owns 16.1% of Nanolive's equity and has a right to designate one board member to Nanolive's board.

The Company evaluated the subsequent events through February 25, 2022, the date the financial statements are available to be issued.

Subsidiaries

Theravance Biopharma US, Inc. (Delaware)

Theravance Biopharma UK Limited (England and Wales)

Theravance Biopharma Ireland Limited (Ireland)

Theravance Biopharma R&D IP, LLC (Delaware)

Theravance Biopharma Antibiotics IP, LLC (Delaware)

Theravance Biopharma US Holdings, Inc. (Delaware)

Triple Royalty Sub LLC (Delaware)

Triple Royalty Sub II LLC (Delaware)

Exhibit 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We consent to the incorporation by reference in the following Registration Statements:

(1) Registration Statements (Form S-8 Nos. 333-198206, 333-202856, 333-210225, 333-216446, 333-223470, 333-231559, 333-236868 and 333-253894) pertaining to the Theravance Biopharma, Inc. 2013 Equity Incentive Plan and the Theravance Biopharma, Inc. 2013 Employee Share Purchase Plan;

(2) Registration Statement (Form S-8 No. 333-200225) pertaining to the Theravance Biopharma, Inc. 2014 New Employee Equity Incentive Plan; and

(3) Registration Statement (Form S-3 Nos. 333-235339 and 333-248534) of Theravance Biopharma, Inc.;

of our reports dated February 28, 2022, with respect to the consolidated financial statements of Theravance Biopharma, Inc. and the effectiveness of internal control over financial reporting of Theravance Biopharma, Inc., included in this Annual Report (Form 10-K) of Theravance Biopharma, Inc. for the year ended December 31, 2021.

/s/ Ernst & Young LLP

Redwood City, California
February 28, 2022

Exhibit 23.2

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We have issued our report dated February 25, 2022, with respect to the financial statements of Theravance Respiratory Company, LLC included in this Annual Report of Theravance Biopharma, Inc. on Form 10-K for the year ended December 31, 2021. We consent to the incorporation by reference of said report in the Registration Statements of Theravance Biopharma, Inc. on Forms S-8 (File No. 333-198206, File No. 333-202856, File No. 333-210225, File No. 333-216446, File No. 333-223470, File No. 333-231559, File No. 333-236868, File No. 333-253894, and File No. 333-200225) and on Forms S-3 (File No. 333-235339, and File No.333-248534).

/s/ GRANT THORNTON LLP

San Francisco, California
February 28, 2022

Exhibit 31.1

Certification of Chief Executive Officer
Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002

I, Rick E Winningham, certify that:

1. I have reviewed this Annual Report on Form 10-K of Theravance Biopharma, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the periods covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the periods in which this report is being prepared;

   b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the periods covered by this report based on such evaluation; and

   d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

February 28, 2022
(Date)

/s/ RICK E WINNINGHAM
Rick E Winningham
Chairman of the Board and Chief Executive Officer
(Principal Executive Officer)

Exhibit 31.2

Certification of Chief Financial Officer
Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002

I, Andrew Hindman, certify that:

1. I have reviewed this Annual Report on Form 10-K of Theravance Biopharma, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the periods covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the periods in which this report is being prepared;

   b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the periods covered by this report based on such evaluation; and

   d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

February 28, 2022
(Date)

/s/ Andrew Hindman
Andrew Hindman
Senior Vice President and Chief Financial Officer
(Principal Financial Officer)

CERTIFICATION OF CHIEF EXECUTIVE OFFICER
PURSUANT TO
18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

I, Rick E Winningham, certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that the Annual Report of Theravance Biopharma, Inc. on Form 10-K for the fiscal year ended December 31, 2021 fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended and that information contained in such Annual Report on Form 10-K fairly presents in all material respects the financial condition of Theravance Biopharma, Inc. for the periods covered by such Annual Report on Form 10-K and results of operations of Theravance Biopharma, Inc. for the periods covered by such Annual Report on Form 10-K.

February 28, 2022
(Date)

By: /s/ Rick E Winningham
Name: Rick E Winningham
Title: *Chairman of the Board and Chief Executive Officer*
(Principal Executive Officer)

CERTIFICATION OF CHIEF FINANCIAL OFFICER
PURSUANT TO
18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

I, Andrew Hindman, certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that the Annual Report of Theravance Biopharma, Inc. on Form 10-K for the fiscal year ended December 31, 2021 fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended and that information contained in such Annual Report on Form 10-K fairly presents in all material respects the financial condition of Theravance Biopharma, Inc. for the periods covered by such Annual Report on Form 10-K and results of operations of Theravance Biopharma, Inc. for the periods covered by such Annual Report on Form 10-K.

February 28, 2022
(Date)

By: /s/ Andrew Hindman
Name: Andrew Hindman
Title: *Senior Vice President and Chief Financial Officer*
(Principal Financial Officer)

A signed original of this written statement required by Section 906 has been provided to Theravance Biopharma, Inc. and will be retained by it and furnished to the Securities and Exchange Commission or its staff upon request.