UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, DC 20549

FORM 8-K

Current Report Pursuant
to Section 13 or 15(d) of the
Securities Exchange Act of 1934

Date of Report (Date of earliest event Reported): **May 4, 2021**

THERAVANCE BIOPHARMA, INC.

(Exact Name of Registrant as Specified in its Charter)

Cayman Islands	**001-36033**	**98-1226628**
(State or Other Jurisdiction of Incorporation)	(Commission File Number)	(I.R.S. Employer Identification Number)

PO Box 309
Ugland House, South Church Street
George Town, Grand Cayman, Cayman Islands KY1-1104
(650) 808-6000
(Addresses, including zip code, and telephone numbers, including area code, of principal executive offices)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (see General Instruction A.2. below):

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Ordinary Share $0.00001 Par Value	TBPH	NASDAQ Global Market

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§ 230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§ 240.12b-2 of this chapter).

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. ☐

Item 2.02. Results of Operations and Financial Condition.

On May 4, 2021, Theravance Biopharma, Inc. issued a press release and is holding a conference call regarding its financial results for the quarter ended March 31, 2021 and a business update. A copy of the press release is furnished as Exhibit 99.1 to this Current Report and a copy of materials that will accompany the call is furnished as Exhibit 99.2 to this Current Report. Additionally, a copy of an Appendix of additional materials is furnished as Exhibit 99.3 to this Current Report.

The information in Item 2.02 and in Item 9.01 of this Current Report on Form 8-K, including Exhibits 99.1, 99.2 and 99.3, is being furnished and shall not be deemed "filed" for the purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Securities Exchange Act of 1934"), or otherwise subject to the liabilities of that Section, nor shall it be incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, except as expressly set forth by specific reference in such a filing.

Item 9.01. Financial Statements and Exhibits.

(d) Exhibits.

99.1	Press Release dated May 4, 2021
99.2	Slide deck entitled First Quarter 2021 Financial Results and Business Update
99.3	Slide deck entitled Appendix May 4, 2021
104	Cover Page Interactive Data File (cover page XBRL tags embedded within the Inline XBRL document)

SIGNATURE

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

THERAVANCE BIOPHARMA, INC.

Date: May 4, 2021

By: /s/ Andrew Hindman
Andrew Hindman
Senior Vice President and Chief Financial Officer

Theravance Biopharma, Inc. Reports First Quarter 2021 Financial Results and Provides Business Update

- Ø *Company completed enrollment for Phase 2 nezulcitinib (TD-0903, COVID lung hyperinflammation) and Phase 2b izencitinib (ulcerative colitis) studies, is near completion of enrollment for ampreloxetine Phase 3, and reaffirms readout timing for these trials*
- Ø *Company updates timing for izencitinib (Crohn's disease) readout to late Q4/early Q1 2022*
- Ø *Company's implied 35% share of YUPELRI® (revefenacin) net sales[1]: $12.9 million*
- Ø *TRELEGY® Q1 2021 global net sales hit a record $341 million, up 37% from Q1 2020. Company is entitled to tiered royalties of 5.5% to 8.5% on TRELEGY net sales[2]*

DUBLIN, IRELAND – MAY 4, 2021 – Theravance Biopharma, Inc. ("Theravance Biopharma" or the "Company") (NASDAQ: TBPH) today reported financial results for the first quarter of 2021.

"2021 is on track to be a transformational year as we make significant progress towards our business goals," said Rick E Winningham, Chief Executive Officer. *"Our commercial assets provide cash flow to invest in our diversified clinical pipeline. GSK's TRELEGY continues an exceptional, unabated growth trajectory. Our YUPELRI team, with our partner Viatris, continues to drive performance despite pandemic-associated headwinds. While we experienced slightly down sequential quarter-over-quarter net sales results, our January 2021 market share was 19%—its highest level since launch—and we ended the quarter on a strong note with March volume demand demonstrating 28% growth over February."*

"Additionally, we are focused on advancing development of our innovative and differentiated pipeline. We continue to progress nezulcitinib, our wholly-owned nebulized lung-selective pan-JAK inhibitor, our potentially best-in-class ampreloxetine for symptomatic neurogenic orthostatic hypotension and izencitinib, our oral gut-selective pan-JAK inhibitor for inflammatory bowel disease that is partnered with Janssen Pharmaceuticals. Our team is looking forward to four significant clinical readouts between now and Q1 2022: our Phase 2 nezulcitinib trial in Q2, our Phase 3 ampreloxetine and Phase 2b izencitinib Ulcerative Colitis trials each in Q3, and the Phase 2 izencitinib Crohn's disease trial in Q4/Q1 2022. We remain committed to delivering each of these clinical data sets with the highest quality as expeditiously as possible."

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[1] *While Viatris Inc. ("Viatris") records the total YUPELRI net sales, the Company is entitled to a 35% share of the profits and losses pursuant to a co-promotion agreement with Viatris.*

[2] *As reported by Glaxo Group Limited or one of its affiliates (GSK); reported sales converted to USD; economic interest related to TRELEGY (the combination of fluticasone furoate, umeclidinium, and vilanterol (FF/UMEC/VI), jointly developed by GSK and Innoviva, Inc.) entitles the Company to upward tiering payments equal to approximately 5.5% to 8.5% on worldwide net sales of the product (net of Theravance Respiratory Company, LLC (TRC) expenses paid and the amount of cash, if any, expected to be used in TRC over the next four fiscal quarters). 75% of the income from the Company's investment in TRC is pledged to service outstanding notes and 25% of income from the Company's investment in TRC is retained by the Company.*

Upcoming Clinical Milestones

- **Q2 2021: Nezulcitinib** (nebulized lung-selective pan-Janus kinase (JAK) inhibitor) Phase 2 for acute hyperinflammation of the lung in COVID-19 (study 0188) – enrollment complete and topline results expected in Q2.
- **Q3 2021: Ampreloxetine** (norepinephrine reuptake inhibitor) Phase 3 for symptomatic neurogenic orthostatic hypotension (study 0169) – enrollment near complete and topline results expected in Q3.
- **Q3 2021: Izencitinib** (gut-selective oral pan-JAK inhibitor for inflammatory intestinal diseases) Phase 2b in ulcerative colitis (study 0157) – enrollment complete and topline results expected in Q3.
- **Q4 2021/Q1 2022: Izencitinib** (gut-selective oral pan-JAK inhibitor for inflammatory intestinal diseases) due to enrollment challenges, Phase 2 in Crohn's disease (study 0173) – enrollment ongoing and topline results now expected in late Q4 2021/early Q1 2022.

Quarterly Highlight

Ø **YUPELRI®** (revefenacin) inhalation solution, the first and only once-daily, nebulized bronchodilator approved in the U.S. for the maintenance treatment of patients with chronic obstructive pulmonary disease (COPD), continued to increase its share of the long-acting nebulized COPD market, increasing to 19.0% in January 2021, up from 18.6% in December 2020.

Economic Interest

- **TRELEGY** (first once-daily single inhaler triple therapy for COPD and asthma)**,** in which the Company holds an economic interest, posted first quarter 2021 global net sales of $341 million (up from $249 million, 36.9%, in the first quarter of 2020); Theravance Biopharma is entitled to tiered royalties of 5.5% to 8.5% of TRELEGY global net sales.[3]

First Quarter Financial Results

- **Revenue:** Total revenue for the first quarter of 2021 was $14.3 million, comprised of non-cash collaboration revenue of $3.9 million primarily attributed to our global collaboration with Janssen and $10.4 million in Viatris collaboration revenue. Total revenue for the first quarter represents a $5.6 million decrease over the same period in 2020.

- **YUPELRI:** The Viatris collaboration revenue of $10.4 million for the first quarter of 2021 represents amounts receivable from Viatris and is comprised of the Company's 35% share of net sales of YUPELRI as well as its proportionate amount of the total shared costs incurred by the two companies. The non-shared YUPELRI costs incurred by Theravance Biopharma are recorded within operating expenses. While Viatris records the total net sales of YUPELRI within its financial statements, our implied 35% share of net sales of YUPELRI for the first quarter of 2021 was $12.9 million.

- **Research and Development (R&D) Expenses:** R&D expenses for the first quarter of 2021 were $67.6 million, compared to $66.0 million in the same period in 2020. First quarter R&D expenses included total non-cash share-based compensation of $7.9 million.

[3] *As reported by Glaxo Group Limited or one of its affiliates (GSK); reported sales converted to USD; economic interest related to TRELEGY (the combination of fluticasone furoate, umeclidinium, and vilanterol (FF/UMEC/VI), jointly developed by GSK and Innoviva, Inc.) entitles the Company to upward tiering payments equal to approximately 5.5% to 8.5% on worldwide net sales of the product (net of Theravance Respiratory Company, LLC (TRC) expenses paid and the amount of cash, if any, expected to be used in TRC over the next four fiscal quarters). 75% of the income from the Company's investment in TRC is pledged to service outstanding notes and 25% of income from the Company's investment in TRC is retained by the Company.*

- **Selling, General and Administrative (SG&A) Expenses:** SG&A expenses for the first quarter of 2021 were $30.6 million, compared to $26.3 million in the same period in 2020. First quarter SG&A expenses included total non-cash share-based compensation of $7.9 million.

- **Operating Loss:** Operating loss for the first quarter of 2021 was $83.9 million compared to $72.5 million in the same period of 2020.

- **Cash Position:** Cash, cash equivalents and marketable securities totaled $210.0 million as of March 31, 2021.

2021 Financial Guidance

- **Operating Expenses** (excluding share-based compensation)**:** The Company expects full year 2021 R&D expense of $195 million to $225 million, and SG&A expense of $80 million to $90 million.

Conference Call and Live Webcast Today at 5 pm ET

Theravance Biopharma will hold a conference call and live webcast accompanied by slides today at 5 pm ET / 2 pm PT / 10 pm IST. To participate, please dial (855) 296-9648 from the U.S. or (920) 663-6266 for international callers, using the confirmation code 1092615. Those interested in listening to the conference call live via the internet may do so by visiting Theravance.com, under the Investors section, Presentations and Events.

A replay will be available on Theravance.com for 30 days through June 3, 2021. An audio replay will also be available through 8:00 pm ET on May 11, 2021, by dialing (855) 859-2056 from the U.S., or (404) 537-3406 for international callers, and then entering confirmation code 1092615.

About Theravance Biopharma

Theravance Biopharma, Inc. is a diversified biopharmaceutical company primarily focused on the discovery, development and commercialization of organ-selective medicines. Its purpose is to pioneer a new generation of small molecule drugs designed to better meet patient needs. Its research is focused in the areas of inflammation and immunology.

In pursuit of its purpose, Theravance Biopharma applies insights and innovation at each stage of its business and utilizes its internal capabilities and those of partners around the world. The Company applies organ-selective expertise to target disease biologically, to discover and develop medicines that may expand the therapeutic index with the goal of maximizing efficacy and limiting systemic side effects. These efforts leverage years of experience in developing lung-selective medicines to treat respiratory disease, including FDA-approved YUPELRI® (revefenacin) inhalation solution indicated for the maintenance treatment of patients with chronic obstructive pulmonary disease (COPD). Its pipeline of internally discovered programs is targeted to address significant patient needs.

Theravance Biopharma has an economic interest in potential future payments from Glaxo Group Limited or one of its affiliates (GSK) pursuant to its agreements with Innoviva, Inc. relating to certain programs, including TRELEGY.

For more information, please visit www.theravance.com.

This press release contains and the conference call will contain certain "forward-looking" statements as that term is defined in the Private Securities Litigation Reform Act of 1995 regarding, among other things, statements relating to goals, plans, objectives, expectations and future events. Theravance Biopharma intends such forward-looking statements to be covered by the safe harbor provisions for forward-looking statements contained in Section 21E of the Securities Exchange Act of 1934 and the Private Securities Litigation Reform Act of 1995. Examples of such statements include statements relating to: the Company's goals, designs, strategies, plans and objectives, the Company's regulatory strategies and timing of clinical studies (including the data therefrom), the potential characteristics, benefits and mechanisms of action of the Company's product and product candidates, the potential that the Company's research programs will progress product candidates into the clinic, the Company's expectations for product candidates through development, the Company's expectations regarding its allocation of resources, potential regulatory approval and commercialization (including their differentiation from other products or potential products), product sales or profit share revenue and the Company's expectations for its expenses, excluding share-based compensation and other financial results. These statements are based on the current estimates and assumptions of the management of Theravance Biopharma as of the date of the press release and the conference call and are subject to risks, uncertainties, changes in circumstances, assumptions and other factors that may cause the actual results of Theravance Biopharma to be materially different from those reflected in the forward-looking statements. Important factors that could cause actual results to differ materially from those indicated by such forward-looking statements include, among others, risks related to: disagreements with Innoviva, Inc. and TRC LLC, the uncertainty of arbitration and litigation and the possibility that the results of these proceedings could be adverse to the Company, delays or difficulties in commencing, enrolling or completing clinical studies, the potential that results from clinical or non-clinical studies indicate the Company's compounds or product candidates are unsafe or ineffective, risks that product candidates do not obtain approval from regulatory authorities, the feasibility of undertaking future clinical trials for our product candidates based on policies and feedback from regulatory authorities, dependence on third parties to conduct clinical studies, delays or failure to achieve and maintain regulatory approvals for product candidates, risks of collaborating with or relying on third parties to discover, develop, manufacture and commercialize products, and risks associated with establishing and maintaining sales, marketing and distribution capabilities with appropriate technical expertise and supporting infrastructure. In addition, while we expect the effects of COVID-19 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 (including but not limited to our later stage clinical programs for izencitinib and ampreloxetine), 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, 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. Other risks affecting Theravance Biopharma are in the Company's Form 10-K filed with the SEC on February 26, 2021 and other periodic reports filed with the SEC. In addition to the risks described above and in Theravance Biopharma's filings with the SEC, other unknown or unpredictable factors also could affect Theravance Biopharma's results. No forward-looking statements can be guaranteed, and actual results may differ materially from such statements. Given these uncertainties, you should not place undue reliance on these forward-looking statements. Theravance Biopharma assumes no obligation to update its forward-looking statements on account of new information, future events or otherwise, except as required by law.

Contact: Gail B. Cohen
Corporate Communications
917-214-6603

THERAVANCE BIOPHARMA, INC.
CONDENSED CONSOLIDATED BALANCE SHEETS
(In thousands)

	March 31, 2021 (Unaudited)	December 31, 2020 (1)
Assets		
Current assets:		
Cash and cash equivalents and short-term marketable securities	$ 209,968	$ 292,941
Receivables from collaborative arrangements	11,915	15,868
Receivables from licensing arrangements	-	-
Amounts due from TRC, LLC	42,359	53,799
Prepaid clinical and development services	18,792	20,374
Other prepaid and current assets	10,037	10,359
Total current assets	293,071	393,341
Property and equipment, net	16,944	16,422
Operating lease assets	42,517	43,260
Equity in net assets of TRC, LLC	19,439	12,750
Restricted cash	833	833
Other assets	2,304	2,451
Total assets	$ 375,108	$ 469,057
Liabilities and Shareholders' Deficit		
Current liabilities	$ 86,492	$ 123,571
Convertible senior notes due 2023, net	227,230	226,963
Non-recourse notes due 2035, net	375,181	372,873
Long-term operating lease liabilities	57,026	47,220
Other long-term liabilities	2,397	2,181
Shareholders' deficit	(373,218)	(303,751)
Total liabilities and shareholders’ deficit	$ 375,108	$ 469,057

(1) The condensed consolidated balance sheet as of December 31, 2020 has been derived from the audited consolidated financial statements included in the Company's Annual Report on Form 10-K for the year ended December 31, 2020.

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

	Three Months Ended March 31,	
	2021	2020
	(Unaudited)	
Revenue:		
Collaboration revenue	$ 3,872	$ 6,632
Licensing revenue	-	1,500
Viatris collaboration agreement	10,385	11,730
Total revenue	14,257	19,862
Costs and expenses:		
Research and development (1)	67,599	66,013
Selling, general and administrative (1)	30,550	26,325
Total costs and expenses	98,149	92,338
Loss from operations	(83,892)	(72,476)
Income from investment in TRC, LLC	16,547	13,515
Interest expense	(11,873)	(9,941)
Loss on extinguishment of debt	-	(15,464)
Interest and other income, net	(234)	1,460
Loss before income taxes	(79,452)	(82,906)
Provision for income tax expense	(227)	(147)
Net loss	$ (79,679)	$ (83,053)
Net loss per share:		
Basic and diluted net loss per share	$ (1.24)	$ (1.40)
Shares used to compute basic and diluted net loss per share	64,493	59,463

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

	Three Months Ended March 31,	
(In thousands)	2021	2020
Research and development	$ 7,921	$ 7,865
Selling, general and administrative	7,911	7,411
Total share-based compensation expense	$ 15,832	$ 15,276

Exhibit 99.2


Theravance Biopharma
Medicines That Make a Difference®
First Quarter 2021
Financial Results and Business Update
May 4, 2021
THERAVANCE BIOPHARMA®, THERAVANCE®, the Cross/Star logo and MEDICINES THAT MAKE A DIFFERENCE® are registered trademarks of the Theravance Biopharma group of companies (in the U.S. and certain other countries).
All third party trademarks used herein are the property of their respective owners.
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Forward-looking statements

Under the safe harbor provisions of the U.S. Private Securities Litigation Reform Act of 1995, the company cautions investors that any forward-looking statements or projections made by the company are subject to risks and uncertainties that may cause actual results to differ materially from the forward-looking statements or projections.

Examples of forward-looking statements in this presentation may include the Company's goals, designs, strategies, plans and objectives, the Company's regulatory strategies and timing of clinical studies (including the data therefrom), the potential characteristics, benefits and mechanisms of action of the Company's product and product candidates, the potential that the Company's research programs will progress product candidates into the clinic, the Company's expectations for product candidates through development, the Company's expectations regarding its allocation of resources, potential regulatory approval and commercialization (including their differentiation from other products or potential products), product sales or profit share revenue and the Company's expectations for its expenses, excluding share-based compensation and other financial results.

The company's forward-looking statements are based on the estimates and assumptions of management as of the date of this presentation and are subject to risks and uncertainties that may cause the actual results to be materially different than those projected, such as risks related to the impacts on the COVID-19 global pandemic on our business, delays or difficulties in commencing, enrolling or completing clinical studies, the potential that results from clinical or non-clinical studies indicate the Company's compounds or product candidates are unsafe or ineffective, risks that product candidates do not obtain approval from regulatory authorities, the feasibility of undertaking future clinical trials for our product candidates based on policies and feedback from regulatory authorities, dependence on third parties to conduct clinical studies, delays or failure to achieve and maintain regulatory approvals for product candidates, risks of collaborating with or relying on third parties to discover, develop, manufacture and commercialize products, and risks associated with establishing and maintaining sales, marketing and distribution capabilities with appropriate technical expertise and supporting infrastructure, disagreements with Innoviva, Inc. and TRC LLC, the uncertainty of arbitration and litigation and the possibility that an arbitration award or litigation result could be adverse to the Company.

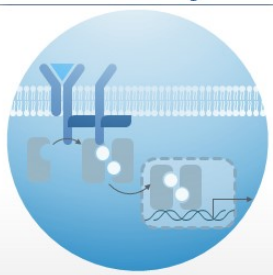
Other risks affecting Theravance Biopharma are in the company's Form 10-K filed with the SEC on February 26, 2021, and other periodic reports filed with the SEC.

Agenda

Introduction	**Gail B. Cohen** Vice President, Corporate Communications
Overview	**Rick E Winningham** Chief Executive Officer
Development and Commercial Update	**Richard A. Graham** Senior Vice President, Development **Frank Pasqualone** Senior Vice President, Chief Business Officer
Financial Update	**Andrew A. Hindman** Senior Vice President, Chief Financial Officer
Closing Remarks	**Rick E Winningham** Chief Executive Officer

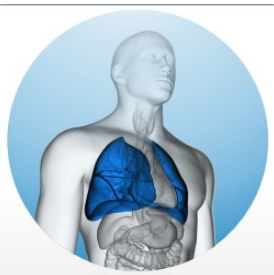
Theravance Biopharma difference: Targeting disease with organ selective medicines

Pathway



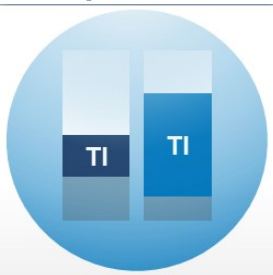
Target disease biology

Disease



Optimize effect in the organ where the disease is active

Therapeutic Index



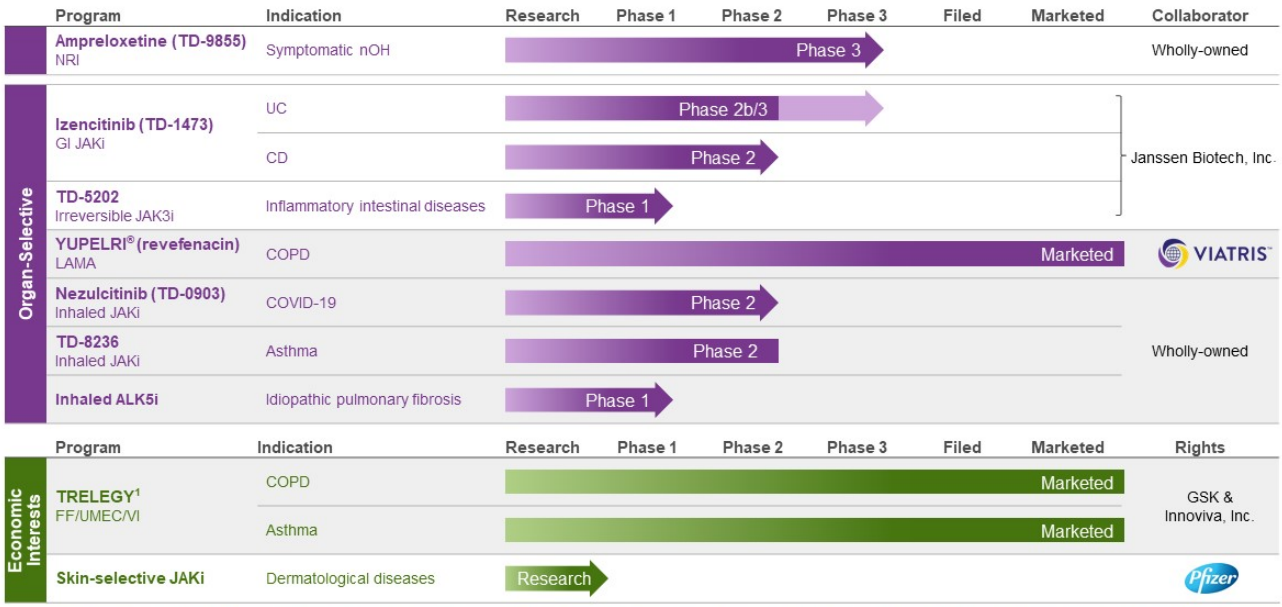
Expand TI with the goal of maximizing efficacy and limiting systemic side effects

Pioneering a new generation of small molecule drugs designed to better meet patient needs

Theravance Biopharma
Medicines That Make a Difference

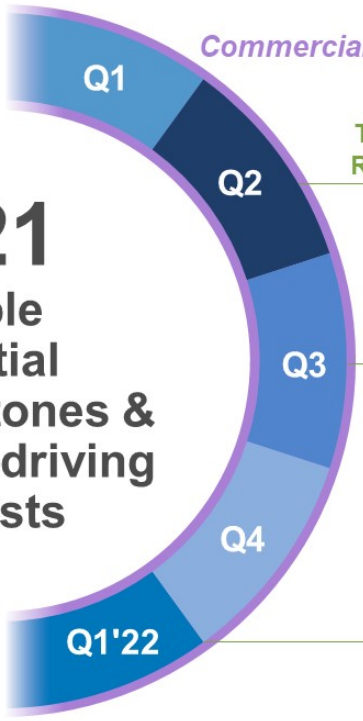
TI, therapeutic index.

Key programs supported by proven development and commercial expertise



1. TBPH holds 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 Agreement over the next four fiscal quarters). 75% of TRC income received is pledged to service outstanding notes, 25% of royalties received retained by TBPH. All statements concerning TRELEGY ELLIPTA based on publicly available information. ALK5i, transforming growth factor β receptor I kinase inhibitor; CD, Crohn's disease; COPD, chronic obstructive pulmonary disease; FF/UMEC/VI, fluticasone furoate/umeclidinium/vilanterol; JAKi, Janus kinase inhibitor; LAMA, long-acting muscarinic receptor antagonist; nOH, neurogenic orthostatic hypotension; NRI, norepinephrine reuptake inhibitor; UC, ulcerative colitis.

Commercial progress of YUPELRI® & GSK's TRELEGY



2021
Multiple potential milestones & value-driving catalysts

TOPLINE RESULTS

Nezulcitinib (TD-0903)
Phase 2 (0188) COVID-19

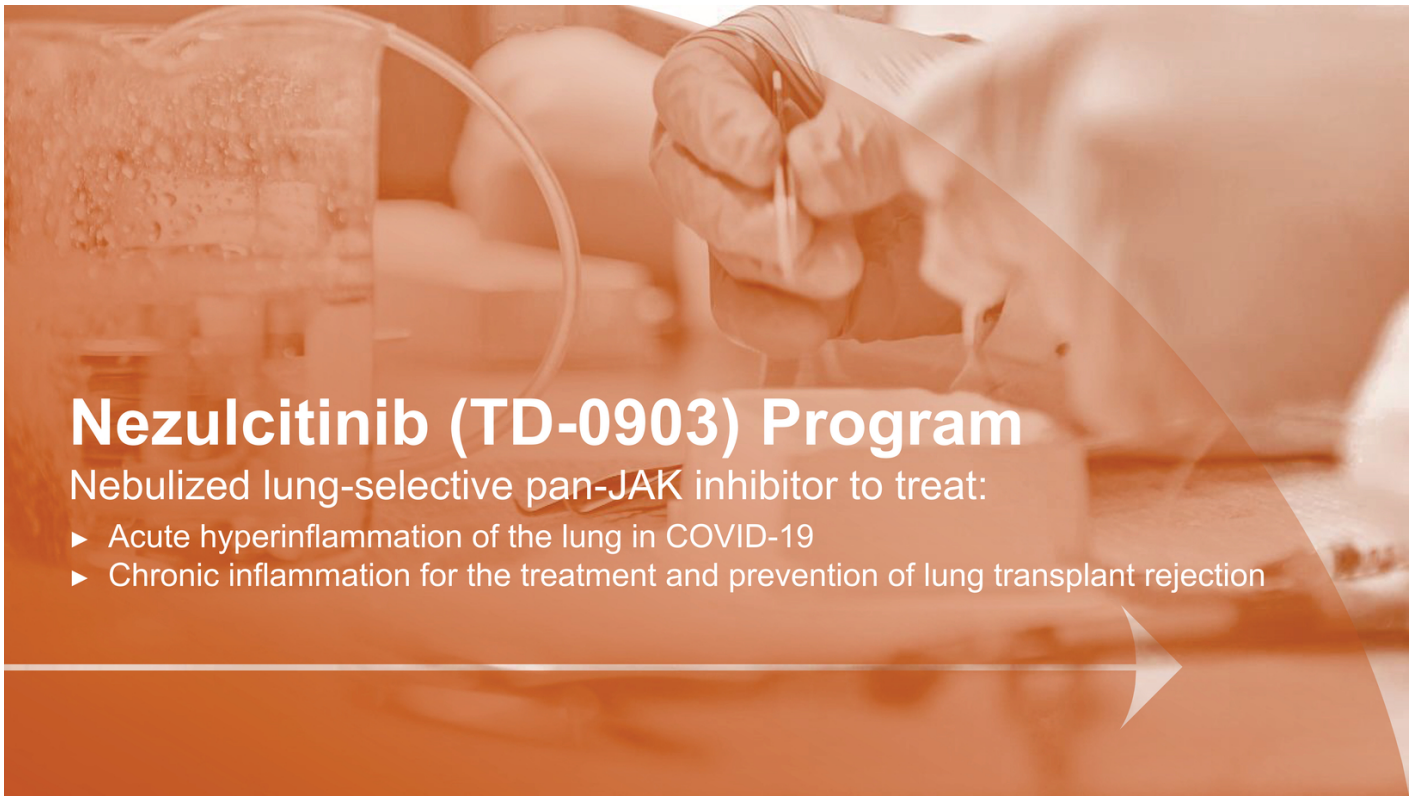
Ampreloxetine
SEQUOIA (0169) Phase 3 symptomatic nOH

Izencitinib
RHEA (0157) Phase 2b ulcerative colitis

Izencitinib
DIONE (0173) Phase 2 Crohn's disease

Theravance Biopharma
MedicinesThat Make a Difference

TBPH holds 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 Agreement over the next four fiscal quarters). 75% of TRC income received is pledged to service outstanding notes, 25% of royalties retained by TBPH. Our non-recourse Triple II 9.5% Fixed Rate Term Notes due on or before 2035. All statements concerning TRELEGY based on publicly available information. TRELEGY is FF/UMEC/VI or fluticasone furoate/umeclidinium/vilanterol; comprised of inhaled corticosteroid, long-acting muscarinic receptor antagonist, and long-acting β2 agonists, active components of Anoro (UMEC/VI). nOH, neurogenic orthostatic hypotension.



Nezulcitinib (TD-0903) Program

Nebulized lung-selective pan-JAK inhibitor to treat:

- Acute hyperinflammation of the lung in COVID-19
- Chronic inflammation for the treatment and prevention of lung transplant rejection

Nezulcitinib (TD-0903): breaking new ground with inhaled JAKi

Focused execution in acute lung injury (ALI) driven by patient need

COVID-19 MARKET DYNAMICS

- >149M COVID-19 patients globally[1]; >32M patients in US[2]
- 56% of US population ≥1 vaccine dose; 40% fully vaccinated[3]
- Virus still surging in communities / parts of the world[1]
- 5 variants of concern in US[4]
- Declining but substantial proportion of population refusing vaccination[5]
- Disproportionate burden on people of color[6]

Treatments needed for hospitalized COVID-19 patients with acute lung injury

TD-0903 Dose finding placebo controlled data[7]

- Generally well-tolerated
- Low systemic exposure
- Positive trend in clinical status, reduced hospital stay
- No deaths in 3, 10 mg cohorts
- Improved oxygenation from baseline to Day 7
- Improved inflammatory biomarkers

Only therapeutic in development with nebulized lung-targeted approach

BUILDING A PIPELINE IN A PRODUCT

Potential areas for exploration:

- ALI in COVID-19 in hospitalized patients
- Preventing progression of lung hyperinflammation that leads to hospitalization
- Accelerated recovery of long-haul COVID-19 patients
- Future applications for coronavirus and influenza inflammation
- Prevention of lung transplant rejection

Theravance Biopharma
Medicines That Make a Difference

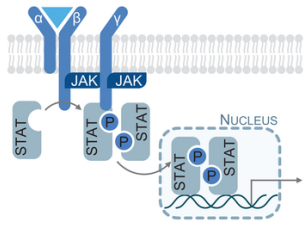
1. https://www.kff.org/coronavirus-covid-19/fact-sheet/coronavirus-tracker/ as of 4.29.21
2. https://coronavirus.jhu.edu/map.html as of 4.25.21
3. https://covid.cdc.gov/covid-data-tracker/#vaccinations as of 5.3.21
4. https://www.cdc.gov/coronavirus/2019-ncov/transmission/variant.html as of 4.2.21
5. https://www.aamc.org/news-insights/herd-immunity-closer-we-think as of 4.25.21
6. https://www.kff.org/coronavirus-covid-19/issue-brief/latest-data-on-covid-19-vaccinations-race-ethnicity/ as of 4.25.21
7. https://www.medrxiv.org/content/10.1101/2021.03.09.21252944v1, n=25

Nezulcitinib: a lung-selective inhaled immunotherapy in development

Broadly inhibits the pulmonary inflammatory cascade caused by viral infection

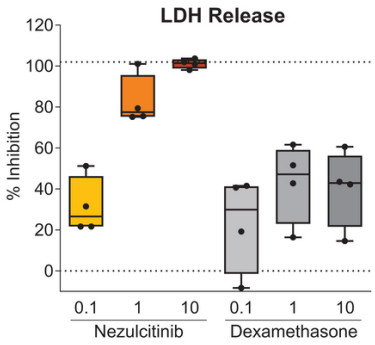
Potential therapeutic benefit via three activities:

Potent pan-JAK inhibition

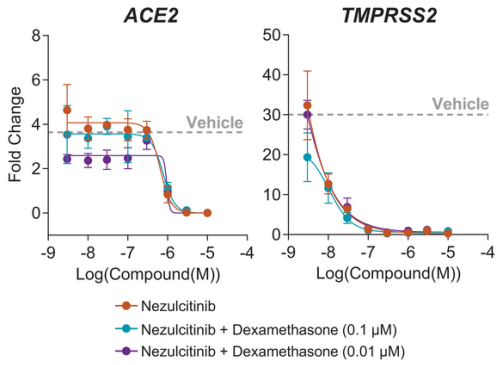


- Suppresses release of key inflammatory markers associated with COVID-19 from epithelial and immune cells (IFNγ, IL-6, IP-10, MCP-1, GM-CSF)

Protection against virus-induced cell death



Prevention of cell entry, limiting virus dissemination in lung



Our goal: nezulcitinib to be the first inhaled treatment to broadly interrupt viral-induced activation and restore immune system balance in the lung

Theravance Biopharma
Medicines That Make a Difference

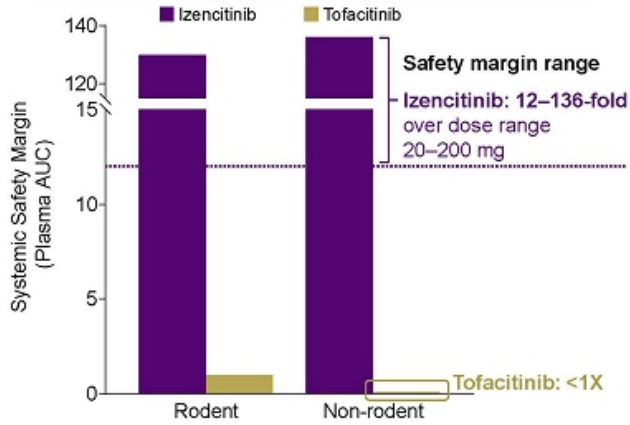
ACE2, angiotensin-converting enzyme 2; GM-CSF, granulocyte-macrophage colony-stimulating factor; IFNγ, interferon gamma; IL-6, interleukin 6; IP-10, IFNγ-induced protein 10; JAK, Janus kinase; LDH, lactate dehydrogenase; MCP-1, monocyte chemoattractant protein-1; STAT, signal transducer and activator of transcription; TMPRSS2, transmembrane protease, serine 2.

Izencitinib (TD-1473/JNJ-8398)

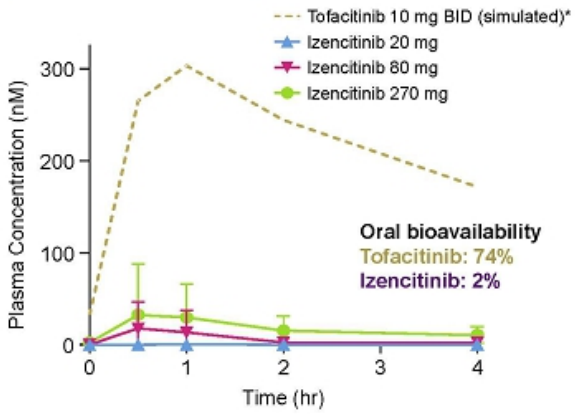
Oral gut-selective pan-JAK inhibitor to treat inflammatory bowel diseases

Izencitinib's oral, gut-selective, pan-JAK approach is designed to reduce systemic side effects

High margins of systemic safety in nonclinical studies



Low systemic plasma concentrations in UC patients



Gut selectivity confers low systemic exposure and offers the potential for reduced adverse effects

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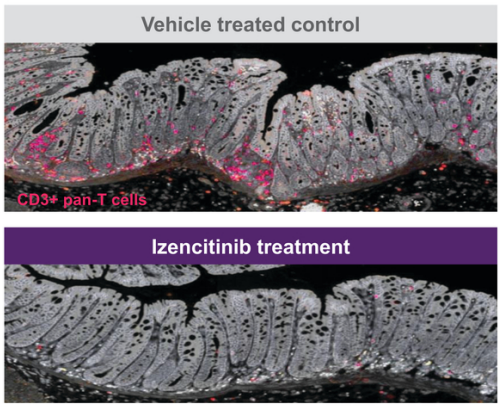
Medicines That Make a Difference

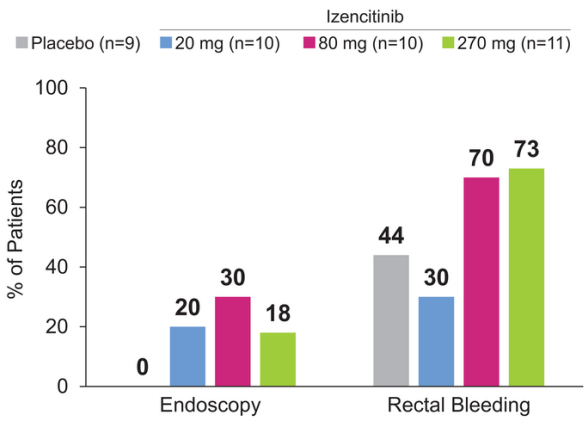
*Simulated tofacitinib concentrations extracted from Dowty ME, et al. J Pharmacol Exp Ther 2014;348:165-73.
AUC, area under curve; BID, twice daily; hr, hour; JAK, Janus kinase; UC, ulcerative colitis.
Margins of safety reflect the ratio of nonclinical to clinical plasma exposures at the highest studied clinical dose (izencitinib) or approved dose (tofacitinib).
Rodent species was rat for izencitinib and tofacitinib; non-rodent species was dog for izencitinib and monkey for tofacitinib.

Izencitinib's oral, gut-selective, pan-JAK approach is designed to maximize efficacy in IBD

Blocks inflammation and penetrates deep within mouse colon



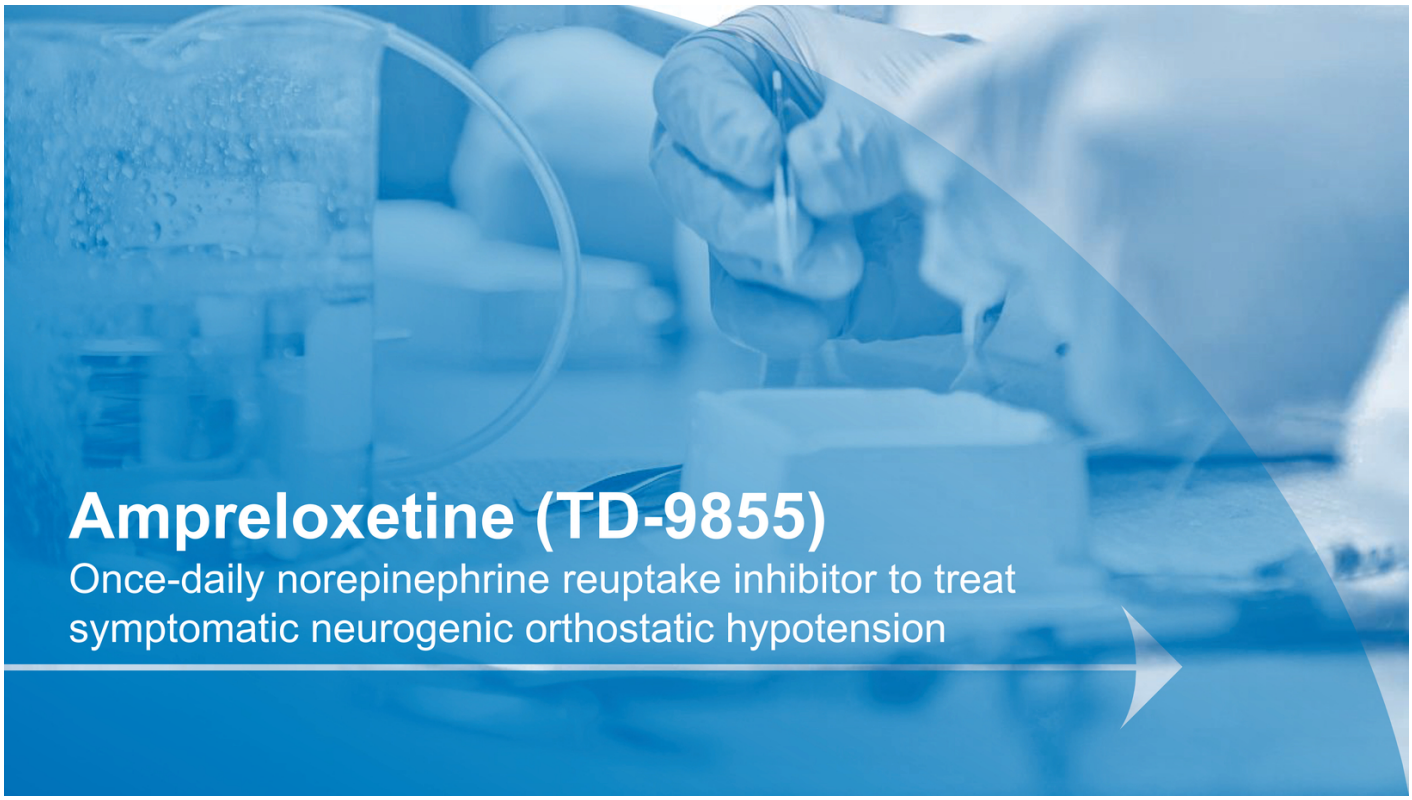
Demonstrates improvement in UC patients in Phase 1b



The gut-selective approach is intended to maximize concentration where it matters, at the site of action in the GI tract

Theravance Biopharma
Medicines That Make a Difference

IBD, inflammatory bowel disease; JAK, Janus kinase; UC, ulcerative colitis. GI, gastrointestinal.



Ampreloxetine (TD-9855)

Once-daily norepinephrine reuptake inhibitor to treat symptomatic neurogenic orthostatic hypotension

Ampreloxetine: new approach in nOH

MARKET DYNAMICS

~350K US patients[1]:
70–80% of MSA patients[2]
30–50% of PD patients[3] have nOH[4]

Specialist network in place: concentrated group of neurologists/ cardiologists treat patients; 'at risk' patients already identified and managed by specialty institutions

Physicians report **urgency to treat** due to high impact on patients' QoL, high risk of injury from falls and caregiver burden

Established nOH Tx paradigm: nOH included in medical treatment guidelines for PD/MSA patients; once diagnosed with nOH, patients prescribed drug

nOH profoundly impacts QoL

Study 0169 primary endpoint:
Change from baseline in OHSA Question 1

OHSA measures core nOH symptom:
Dizziness / lightheadedness due to brain hypoperfusion

Clinically significant endpoint: 1-point OHSA improvement

SYMPTOMS

- Dizziness or lightheadedness
- Fatigue
- Difficulty walking
- Weakness
- Impaired cognition
- Pain (back of head/neck/shoulders)
- Blurred vision
- Tremulousness
- Vertigo

IMPACT

Depression
Social isolation
Poor QoL
Falls (fractures/head trauma)
Morbidity

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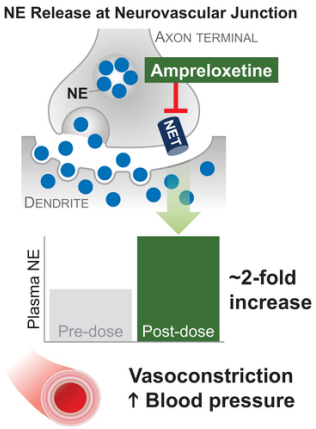
Medicines That Make a Difference

1. https://www.parkinson.org/Understanding-Parkinsons/Statistics; https://www.ninds.nih.gov/Disorders/Patient-Caregiver-Education/Fact-Sheets/Multiple-System-Atrophy.
2. Claassen DO, et al. BMC Neurol 2018;18:125 https://doi.org/10.1186/s12883-018-1129-x. 3. Low PA. AMJC 2015;21:13,October 30 https://www.ajmc.com/view/ace0034_oct15_noh_low. 4. Not all patients are treated with prescription medication.
MSA, multiple system atrophy; nOH, neurogenic orthostatic hypotension; OHSA, orthostatic hypotension symptom assessment; PD, Parkinson's disease; QoL, quality of Life; Tx, treatment.

Ampreloxetine: a once-daily, potent and selective norepinephrine reuptake inhibitor with a differentiated MOA for treating nOH

Ampreloxetine is designed to target and correct the norepinephrine imbalance…

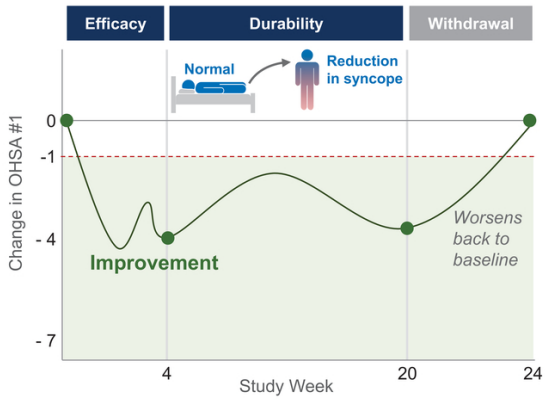


…with potential for market differentiation…

Current nOH treatment options:

- No durable effect
- Multiple daily dosing
- Black box warning for SH

…and demonstrated a clinically meaningful and durable impact[1]



Our goal: ampreloxetine to be the first treatment to demonstrate a sustained impact for patients managing the chronic and debilitating symptoms of nOH

Theravance Biopharma
Medicines That Make a Difference

1. Kaufmann H, et al. Mov Disord. 2019;34(suppl 2). Poster presented at the 2019 International Congress of Parkinson's and Movement Disorder Society.
Note: a 1-point change in the OHSA#1 score is considered clinically meaningful.
MOA, mechanism of action; NE, norepinephrine; NET, norepinephrine transporters; nOH neurogenic orthostatic hypotension; OHSA #1, orthostatic hypotension symptom assessment question #1; SH, supine hypertension.


YUPELRI®
revefenacin inhalation solution
FDA-approved for the maintenance treatment of COPD
First and only once-daily, nebulized maintenance medicine for COPD

YUPELRI® (revefenacin) inhalation solution

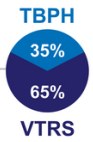
FDA-approved for the maintenance treatment of COPD
First and only once-daily, nebulized maintenance medicine for COPD

Once-daily LAMAs are first-line therapy for moderate-to-very severe COPD[1]

9% of COPD patients (~800,000) use nebulizers for ongoing maintenance therapy; 41% use nebulizers at least occasionally for bronchodilator therapy[2]

TBPH and **VTRS** worldwide strategic collaboration to develop and commercialize nebulized YUPELRI® (revefenacin)

Theravance Biopharma + VIATRIS™

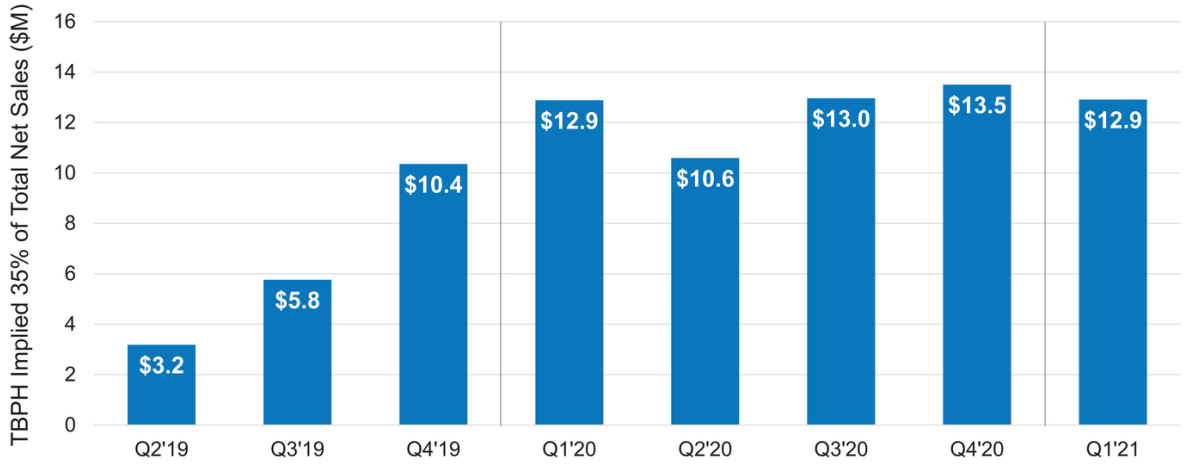


Companies co-promote under US profit/loss share

Theravance Biopharma
Medicines That Make a Difference

1. Global Strategy for Diagnosis, Management, and Prevention of COPD, 2018.
2. TBPH market research (N = 160 physicians); refers to US COPD patients.
COPD, chronic obstructive pulmonary disease; LAMA, long-acting muscarinic antagonist.

TBPH implied 35% of YUPELRI® US net sales by quarter

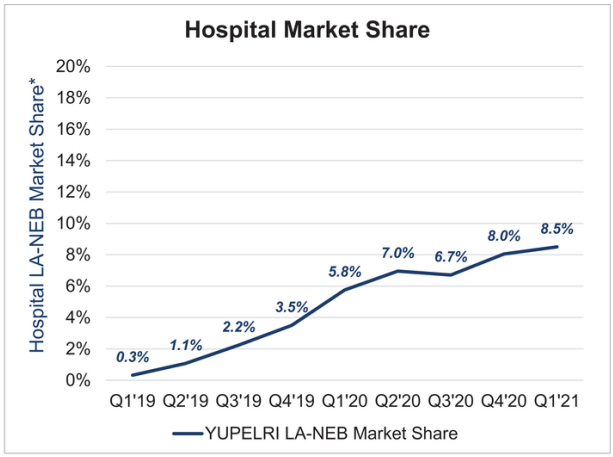


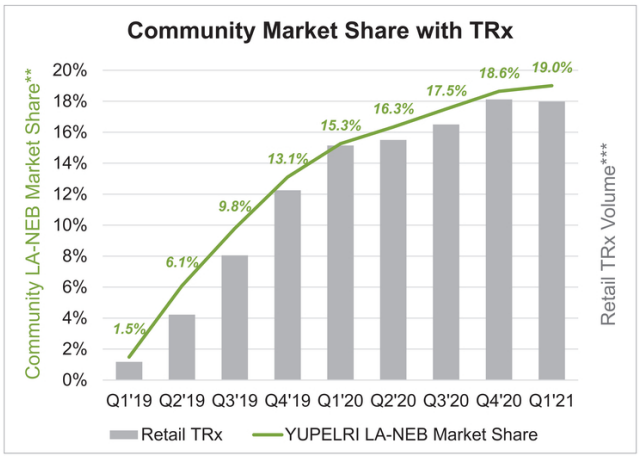
TBPH implied 35% of YUPELRI US net sales represents TBPH's portion of the combined TBPH and VIATRIS net revenue

See TBPH 10K filed February 26, 2021 for greater detail re TBPH implied 35%.

YUPELRI® hospital sales and community TRx trends

Continued market share growth across both the hospital and retail channels





Most patients who receive YUPELRI® in the hospital are discharged with an Rx[1]

TRx volume represents retail only which is typically 33% of Retail + DME

**Community LA-NEB Market Share includes Retail + DME / Med B FFS through January '21

LA-NEB Market: YUPELRI, BROVANA, LONHALA, PERFOROMIST

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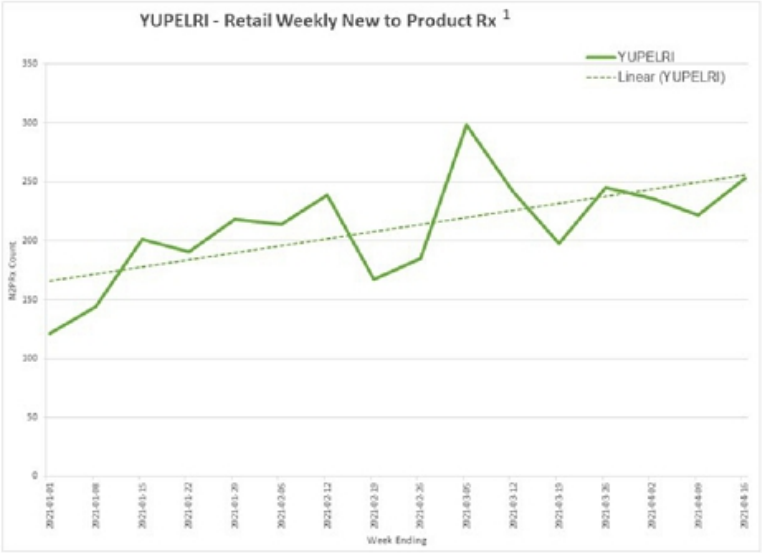
Medicines That Make a Difference

1. Joint VTRS/TBPH Market Research.
* Hospital LA-NEB Market Share - IQVIA DDD through 03/31/2021.
** Community LA-NEB Market Share - IQVIA XPO Excl. LTC (Retail) and SolutionsRx (DME / Med B FFS) through 1/31/2021 (Q1'21 Community LA-NEB Market Share Incomplete).
*** Retail TRx Volume - Symphony Health METYS Prescription Dashboard through 3/31/2021.

Positive growth trends for YUPELRI® continuing beyond March



Increasing New Patient Starts Continue to Drive LA-NEB Market Share Growth

YUPELRI

- 719 hospital accounts have ordered[2]
  - 67% have ordered more than once
- 91% formulary win rate[3]
- Highest number of formulary support presentations in Q1'21 since launch
- 74% commercial coverage[4]

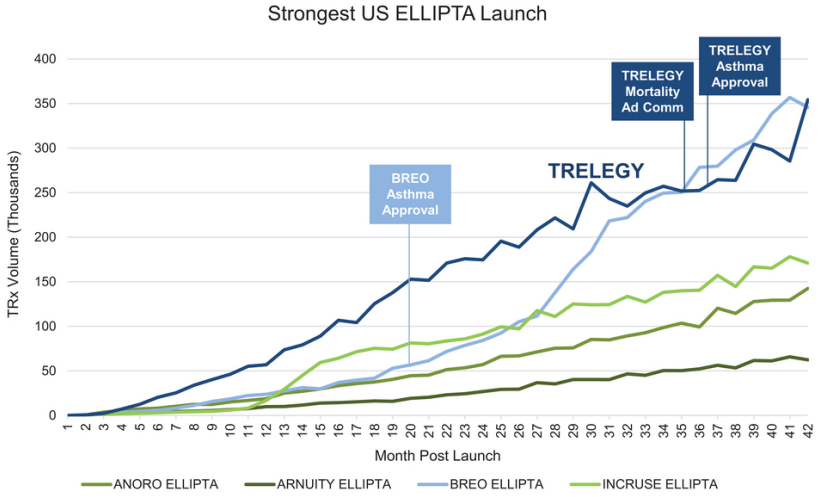
Theravance Biopharma
Medicines That Make a Difference

1. Symphony Health, Metys, Jan – Apr 2021, Weekly New to Product (N2P) Rx Volume.
2. IQVIA DDD through March 2021.
3. TIPH Commercial Data Warehouse.
4. Decision Resources Group (DRG) as of May 2021.


Economic interest
GSK's TRELEGY ELLIPTA (FF/UMEC/VI):
First and only once-daily single inhaler triple therapy

Economic interest in GSK's TRELEGY

Upward-tiering royalties of ~5.5–8.5% of worldwide net sales[1]



Launched in US in November 2017

TRELEGY

- Q1 net sales of $341MM
- Year-over-year sales growth of 37% from the same period in 2020
- US sales ($238MM) benefited from new asthma indication approved and launched in Q3 2020
- International and EU sales grew to $103M; asthma indication approved in Japan in Q4 2020

Source: GSK, Symphony Health Metys monthly TRx data. Source: Symphony Health, Metys, September 2013 – March 2021, Monthly TRx Volume

1. TBPH holds 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 Agreement over the next four fiscal quarters). 75% of TRC income received is pledged to service outstanding notes, 25% of royalties retained by TBPH. Our non-recourse Triple II 9.5% Fixed Rate Term Notes are due on or before 2035. All statements concerning TRELEGY based on publicly available information. TRELEGY is FF/UMEC/VI or fluticasone furoate/umeclidinium/vilanterol; comprised of inhaled corticosteroid, long-acting muscarinic receptor antagonist, and long-acting β2 agonists, active components of Anoro (UMEC/VI).

First quarter 2021 financial highlights

$210.0 million cash[1] as of March 31, 2021

($, in thousands)	Three Months Ended March 31, 2021	2020
	(Unaudited)	
Revenue:		
Collaboration revenue	$ 3,872	$ 6,632
Licensing revenue	-	1,500
Viatris collaboration agreement	10,385	11,730
Total revenue	14,257	19,862
Costs and expenses:		
Research and development[2]	67,599	66,013
Selling, general and administrativet[2]	30,550	26,325
Total costs and expenses	98,149	92,338
Loss from operations	**(83,892)**	**(72,476)**
Share-based compensation expense:		
Research and development	7,921	7,865
Selling, general and administrative	7,911	7,411
Total share-based compensation expense	15,832	15,276
Operating expense excluding share-based compensation:		
Research and development operating expense excluding share-based compensation	59,678	58,148
Selling, general and administrative operating expense excluding share-based compensation	$ 22,639	$ 18,914

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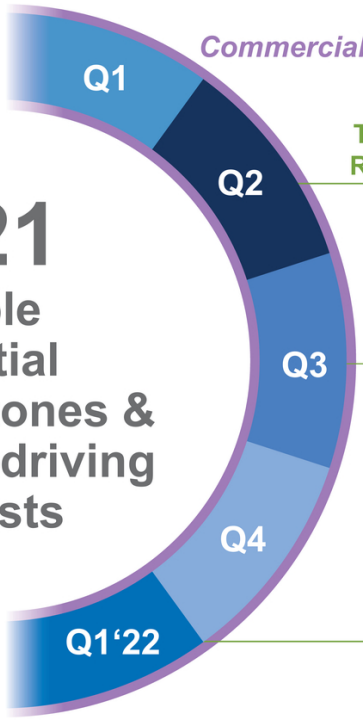
Medicines That Make a Difference

1. Cash, cash equivalents and marketable securities.
2. Amounts include share-based compensation.

Commercial progress of YUPELRI® & GSK's TRELEGY



2021

Multiple potential milestones & value-driving catalysts

TOPLINE RESULTS

Nezulcitinib (TD-0903)
Phase 2 (0188) COVID-19

Ampreloxetine
SEQUOIA (0169) Phase 3 symptomatic nOH

Izencitinib
RHEA (0157) Phase 2b ulcerative colitis

Izencitinib
DIONE (0173) Phase 2 Crohn's disease

Theravance Biopharma
Medicines That Make a Difference

TBPH holds 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 Agreement over the next four fiscal quarters). 75% of TRC income received is pledged to service outstanding notes, 25% of royalties retained by TBPH. Our non-recourse Triple II 9.5% Fixed Rate Term Notes due on or before 2035. All statements concerning TRELEGY based on publicly available information. TRELEGY is FF/UMEC/VI or fluticasone furoate/umeclidinium/vilanterol; comprised of inhaled corticosteroid, long-acting muscarinic receptor antagonist, and long-acting β2 agonists, active components of Anoro (UMEC/VI).°); nOH neurogenic orthostatic hypotension.


Rick E Winningham
Chairman and Chief Executive Officer
Andrew A. Hindman
Senior Vice President, Chief Financial Officer
Frank Pasqualone
Senior Vice President, Chief Business Officer
Q&A Session
Richard A. Graham
Senior Vice President, Development


Theravance
Biopharma
Medicines That Make a Difference®

About YUPELRI® (revefenacin) inhalation solution

YUPELRI® (revefenacin) inhalation solution is a once-daily nebulized LAMA approved for the maintenance treatment of COPD in the US.

Market research by Theravance Biopharma indicates approximately 9% of the treated COPD patients in the US use nebulizers for ongoing maintenance therapy.[1] LAMAs are a cornerstone of maintenance therapy for COPD and YUPELRI® is positioned as the first once-daily single-agent bronchodilator product for COPD patients who require, or prefer, nebulized therapy. YUPELRI®'s stability in both metered dose inhaler and dry powder device formulations suggest that this LAMA could also serve as a foundation for novel handheld combination products.

1. TBPH market research (N=160 physicians); refers to US COPD patients.
COPD, chronic obstructive pulmonary disease; LAMA, long-acting muscarinic antagonist.

YUPELRI® (revefenacin) inhalation solution

YUPELRI® inhalation solution is indicated for the maintenance treatment of patients with chronic obstructive pulmonary disease (COPD).

Important Safety Information (US)

YUPELRI is contraindicated in patients with hypersensitivity to revefenacin or any component of this product.

YUPELRI should not be initiated in patients during acutely deteriorating or potentially life-threatening episodes of COPD, or for the relief of acute symptoms, i.e., as rescue therapy for the treatment of acute episodes of bronchospasm. Acute symptoms should be treated with an inhaled short-acting beta2-agonist.

As with other inhaled medicines, YUPELRI can produce paradoxical bronchospasm that may be life-threatening. If paradoxical bronchospasm occurs following dosing with YUPELRI, it should be treated immediately with an inhaled, short-acting bronchodilator. YUPELRI should be discontinued immediately and alternative therapy should be instituted.

YUPELRI should be used with caution in patients with narrow-angle glaucoma. Patients should be instructed to immediately consult their healthcare provider if they develop any signs and symptoms of acute narrow-angle glaucoma, including eye pain or discomfort, blurred vision, visual halos or colored images in association with red eyes from conjunctival congestion and corneal edema.

Worsening of urinary retention may occur. Use with caution in patients with prostatic hyperplasia or bladder-neck obstruction and instruct patients to contact a healthcare provider immediately if symptoms occur.

Immediate hypersensitivity reactions may occur after administration of YUPELRI. If a reaction occurs, YUPELRI should be stopped at once and alternative treatments considered.

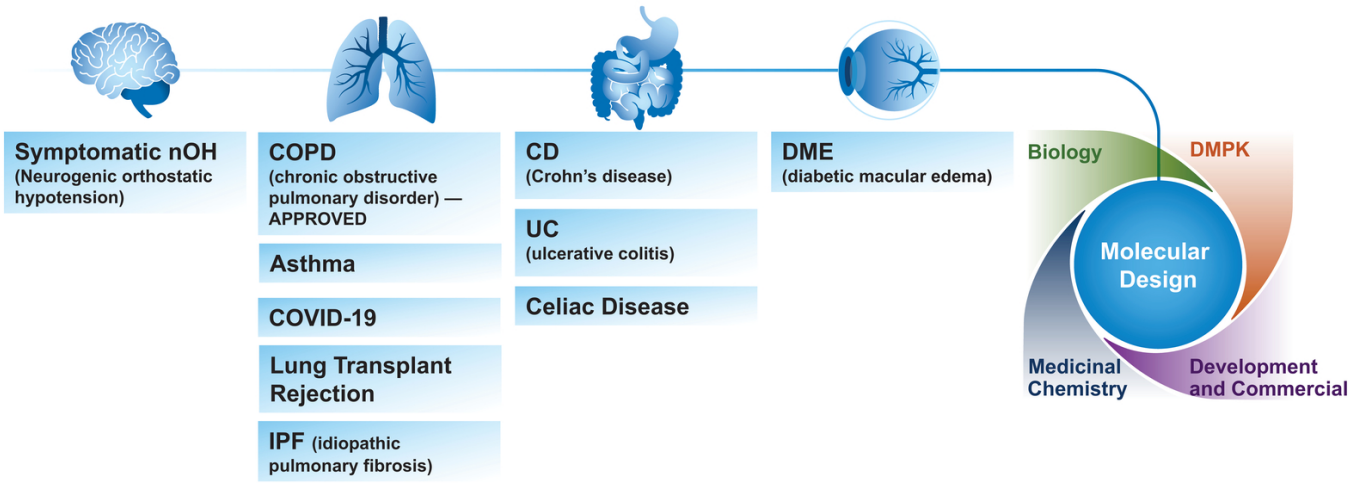
The most common adverse reactions occurring in clinical trials at an incidence greater than or equal to 2% in the YUPELRI group, and higher than placebo, included cough, nasopharyngitis, upper respiratory infection, headache and back pain.

Coadministration of anticholinergic medicines or OATP1B1 and OATP1B3 inhibitors with YUPELRI is not recommended.

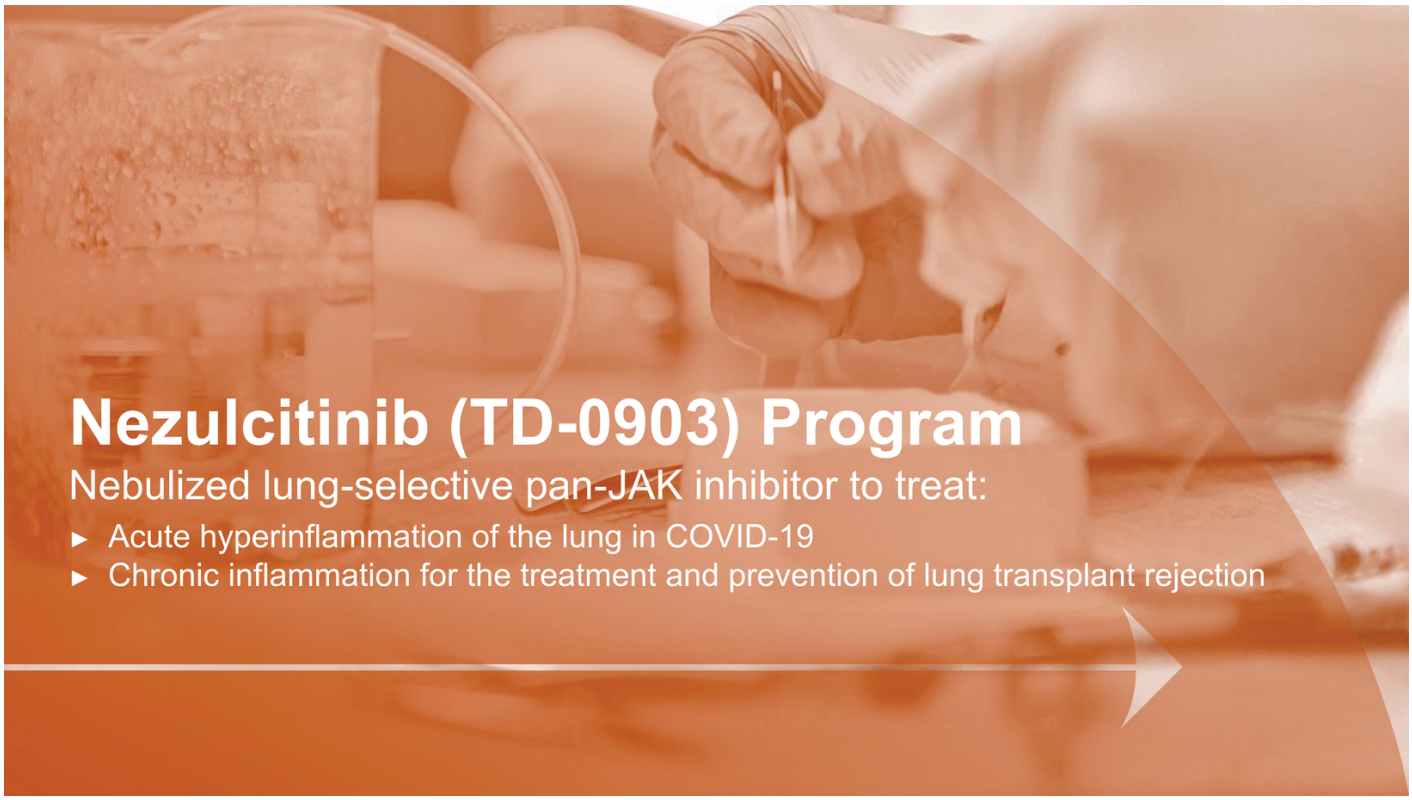
YUPELRI is not recommended in patients with any degree of hepatic impairment.

OATP, organic anion transporting polypeptide.

Research and development portfolio of designed molecules: brain, lung, GI and eye



DMPK, drug metabolism and pharmacokinetics; GI, gastrointestinal.

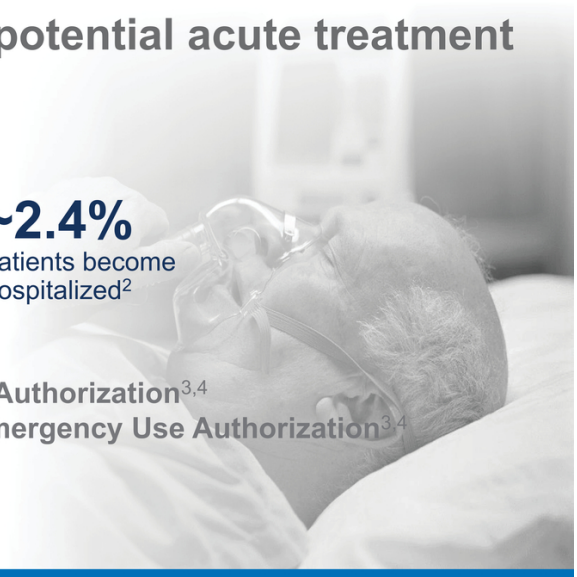


Nezulcitinib (TD-0903) Program

Nebulized lung-selective pan-JAK inhibitor to treat:

- Acute hyperinflammation of the lung in COVID-19
- Chronic inflammation for the treatment and prevention of lung transplant rejection

Leveraging respiratory expertise for potential acute treatment in response to a global pandemic



PATIENT POPULATION

>149M patients worldwide[1]

>32M US patients[1] → **~2.4%** patients become hospitalized[2]

CURRENT US TREATMENT LANDSCAPE

3 vaccines available via Emergency Use Authorization[3,4]
1 approved treatment; 10 available via Emergency Use Authorization[3,4]

STRATEGIC OPPORTUNITY

TD-0903

Inhaled lung-specific therapeutic: potential to be used in combination with other treatment modalities (e.g., antivirals) to provide additional therapeutic benefit with reduced risk of systemic immunosuppressive issues that may occur with systemic anti-inflammatories

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Medicines That Make a Difference

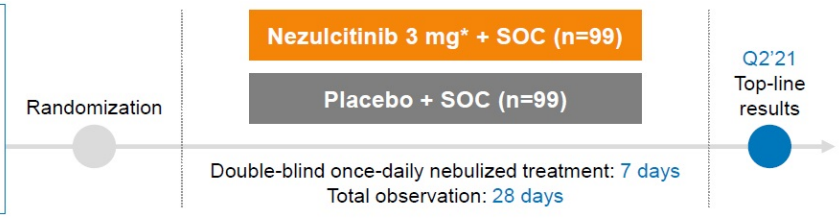
1. https://coronavirus.jhu.edu/map.html, number as of 4/29. 2. IHME. 3. https://www.fda.gov/drugs/coronavirus-covid-19-drugs/coronavirus-treatment-acceleration-program-ctap#dashboard
4. https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization#othercurrenteuas

Nezulcitinib: Randomized, double-blind, placebo-controlled Ph 2 study in hospitalized patients with COVID-19 requiring oxygen support

Part 2 Study 0188

Key inclusion criteria: Hospitalized patients aged 18–80 y requiring supplemental oxygen to maintain >90% saturation (not requiring IMV) with positive SARS-CoV-2 test <72 h prior to randomization and symptom onset >2–10 d prior to hospitalization

Countries: SA, EUR, UK, USA



Objectives

- **Primary:** Number of respiratory-free days from randomization through Day 28
- **Secondary:** Tolerability, PK
- **Exploratory**: Clinical status, duration of hospitalization, repeat-dose safety

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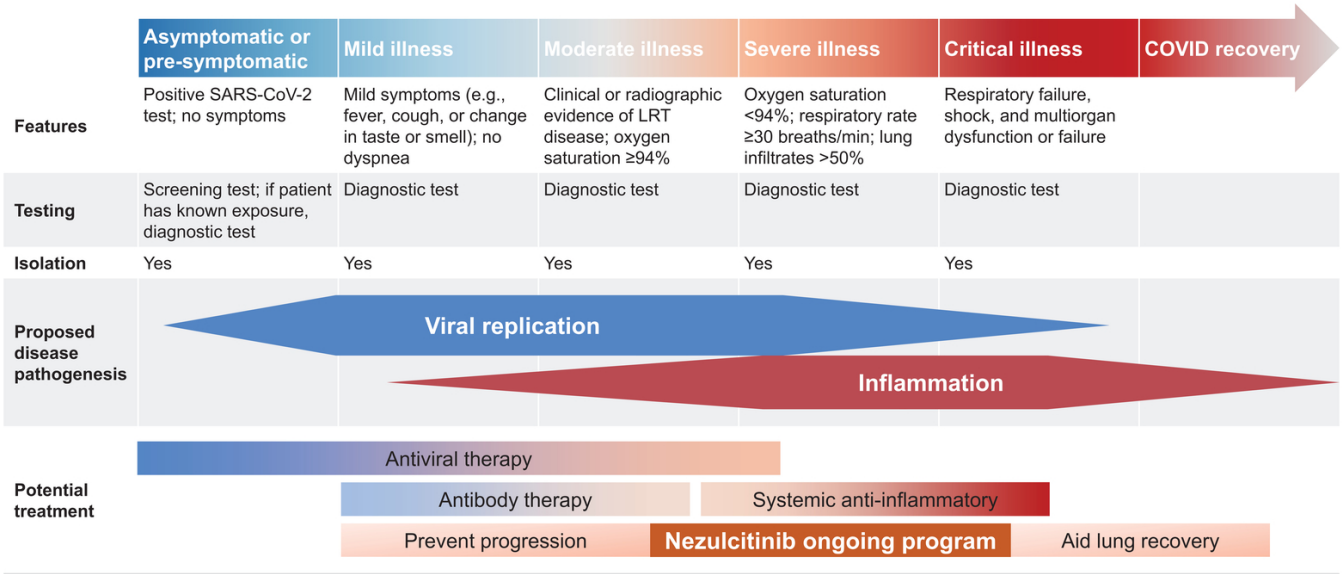
*Loading dose (double the standard dose) administered on Day 1.
NCT04402866
IMV, invasive mechanical ventilation; PK, pharmacokinetics; SARS-CoV-2, Severe acute respiratory syndrome coronavirus 2; SOC, standard of care, includes remdesivir, dexamethasone, anticoagulation.

Potential for nezulcitinib to improve lung immune system balance across disease progression



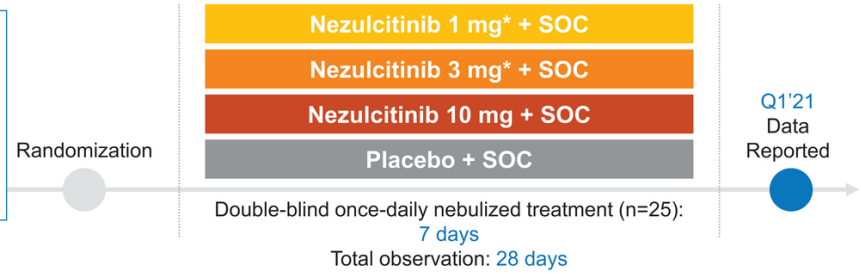
LRT, lower respiratory tract; SARS-CoV-2, Severe acute respiratory syndrome coronavirus 2.

Nezulcitinib: Phase 2 study in hospitalized patients with COVID-19 requiring oxygen support

Dose Finding Data Study 0188

Key inclusion criteria: Hospitalized patients aged 18–80 y requiring supplemental oxygen to maintain >90% saturation (not requiring IMV) with positive SARS-CoV-2 test <72 h prior to randomization and symptom onset >2–10 d prior to hospitalization

Countries: SA, EUR, UK, USA



Objectives

- **Primary:** Repeat-dose safety, tolerability, PK, oxygenation and biomarkers

Results

- Nezulcitinib was generally well-tolerated, with no drug-related SAEs
- Low, dose-dependent systemic exposure at all doses
- Positive trend vs placebo in improving clinical status, oxygenation and reducing hospital stay
- No deaths in nezulcitinib 3 and 10 mg cohorts vs 2 on placebo and 1 in 1 mg cohort

Theravance Biopharma
Medicines That Make a Difference

*Loading dose (double the standard dose) administered on Day 1.
NCT04402866
https://www.medrxiv.org/content/10.1101/2021.03.09.21252944v1
IMV, invasive mechanical ventilation; PK, pharmacokinetics; SAEs, serious adverse events; SARS-CoV-2, Severe acute respiratory syndrome coronavirus 2; SOC, standard of care.

Executive Summary

Overall conclusions from Nezulcitinib Phase 2 dose finding data Study 0188

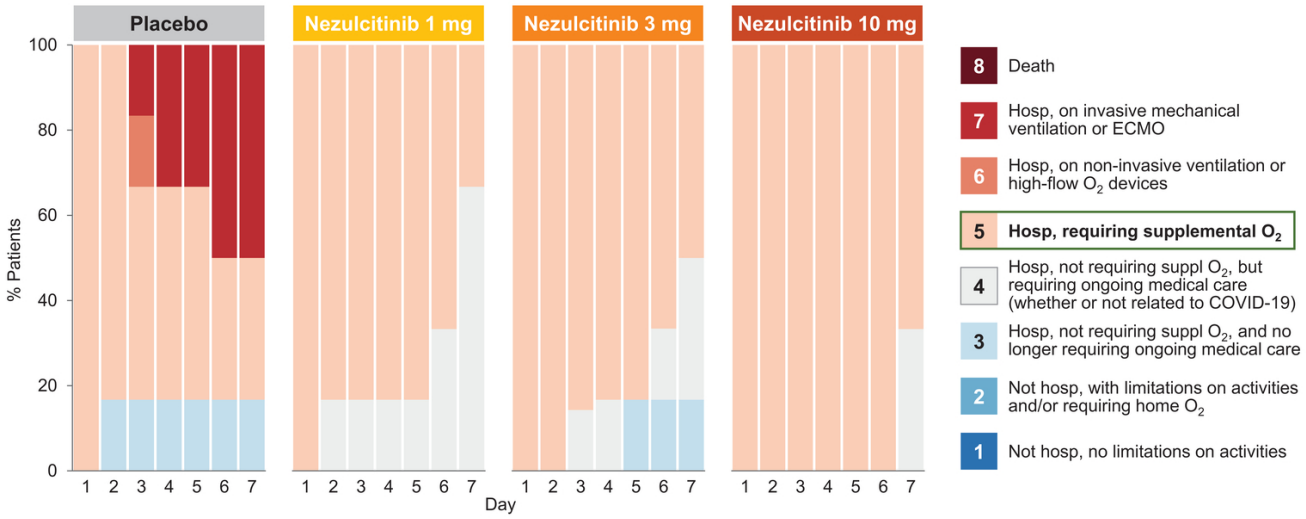
Safety & Tolerability Findings	▸ Nezulcitinib was generally well-tolerated ▸ There were no drug-related serious adverse events ▸ One patient discontinued treatment on 10 mg dose because of isolated elevated liver function value
PK Data	▸ Low, dose-dependent systemic exposure at all doses of nebulized nezulcitinib
Exploratory Clinical Observations	▸ Positive trend vs placebo in improving clinical status and reducing hospital stay ▸ No deaths in 3 mg and 10 mg cohorts vs 2 on placebo and 1 in 1 mg cohort ▸ Nezulcitinib improved oxygenation (S/F ratio) from baseline to Day 7 ▸ Nezulcitinib reduced several relevant inflammatory biomarkers vs placebo, including CRP, IL-10 and RAGE

https://www.medrxiv.org/content/10.1101/2021.03.09.21252944v1

CRP, C-reactive protein; IL, interleukin; PK, pharmacokinetics; RAGE, receptor for advanced glycation end-products; S/F ratio, ratio of oxygen saturation in the blood vs the flow of oxygen administered to the patient.

Nezulcitinib appears to stabilize clinical status within 7 days, compared to placebo

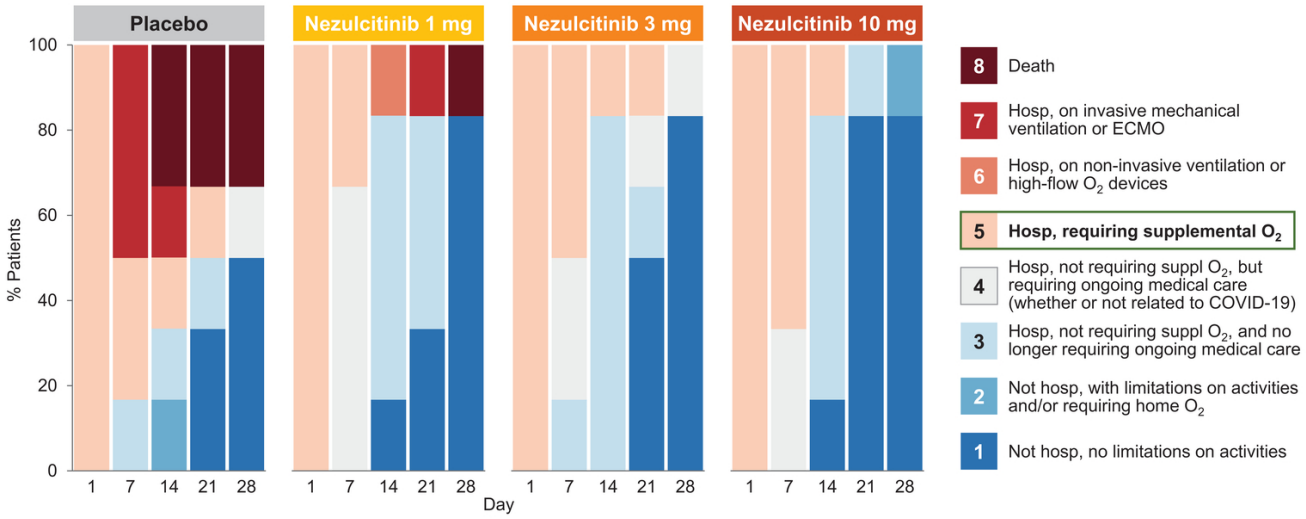
- Nezulcitinib showed a positive trend toward more clinical improvement
- 50% of placebo patients required mechanical ventilation by Day 6



Placebo pooled from Cohorts 1–3.
https://www.medrxiv.org/content/10.1101/2021.03.09.21252944v1
ECMO, extracorporeal membrane oxygenation; Hosp, hospitalized; Suppl, supplemental.

Nezulcitinib shows numerical improvement in clinical status compared to placebo through 28 days

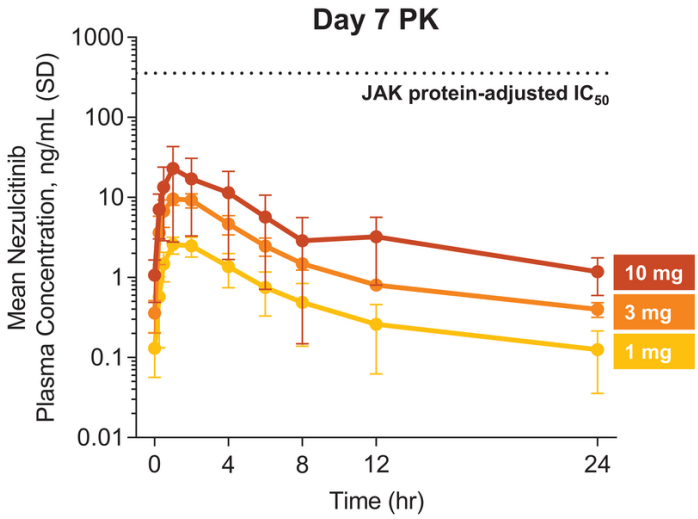
- 2 deaths on placebo and 1 death on 1 mg, but none on 3 and 10 mg groups
- More patients out of hospital and with no limitations by Day 28 with nezulcitinib than placebo



Placebo pooled from Cohorts 1–3.
https://www.medrxiv.org/content/10.1101/2021.03.09.21252944v1
ECMO, extracorporeal membrane oxygenation; Hosp, hospitalized; Suppl, supplemental.

Nezulcitinib lung-selective profile demonstrates low plasma exposure

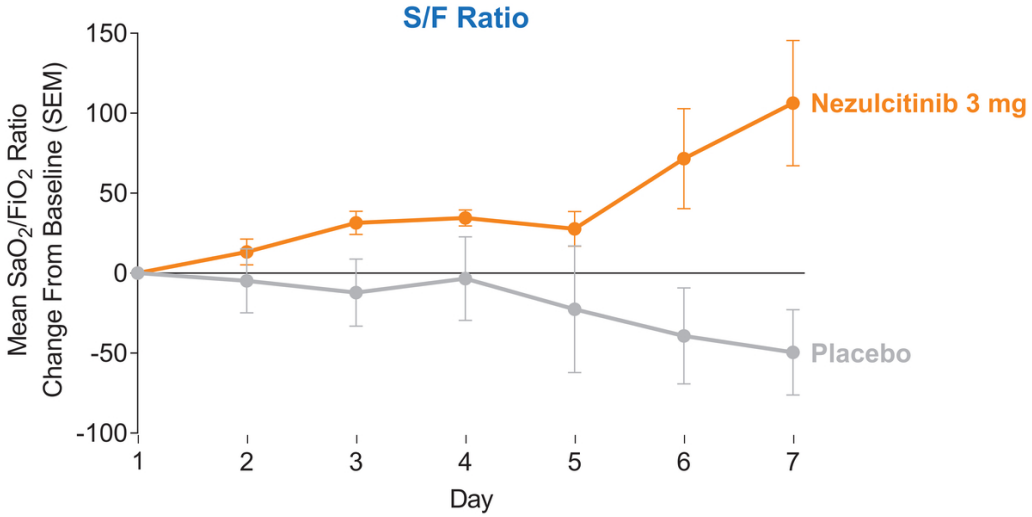
- Day 7 steady-state exposures of nezulcitinib approximately dose proportional
- Initial loading dose on Day 1 for 1 mg and 3 mg doses in order to achieve near-steady-state exposures as quickly as possible
- Plasma exposures were low relative to estimated IC_{50} for systemic JAK inhibition



https://www.medrxiv.org/content/10.1101/2021.03.09.21252944v1

Hr, hour; IC_{50}, inhibitory concentration at which 50% of JAK signaling is blocked; JAK, Janus kinase; PK, pharmacokinetics; SD, standard deviation.

Nezulcitinib 3 mg showed positive trend in improving blood oxygenation versus placebo as measured by S/F Ratio



Nezulcitinib 3 mg progressed to Phase 2 Part 2 with data expected Q2 2021

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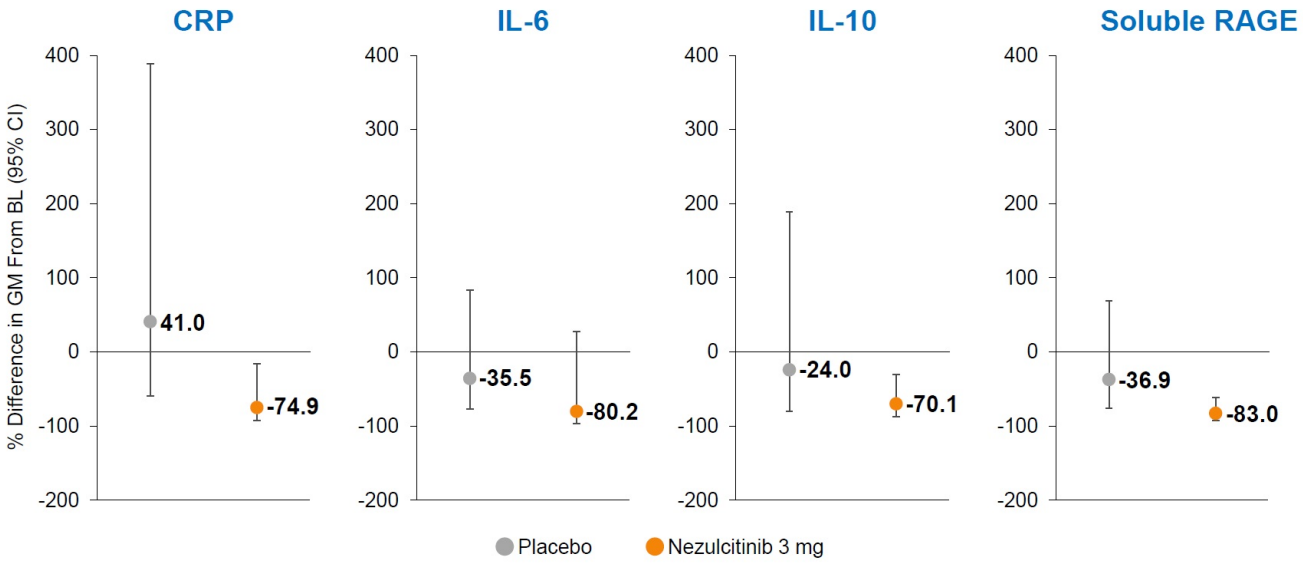
Medicines That Make a Difference

https://www.medrxiv.org/content/10.1101/2021.03.09.21252944v1

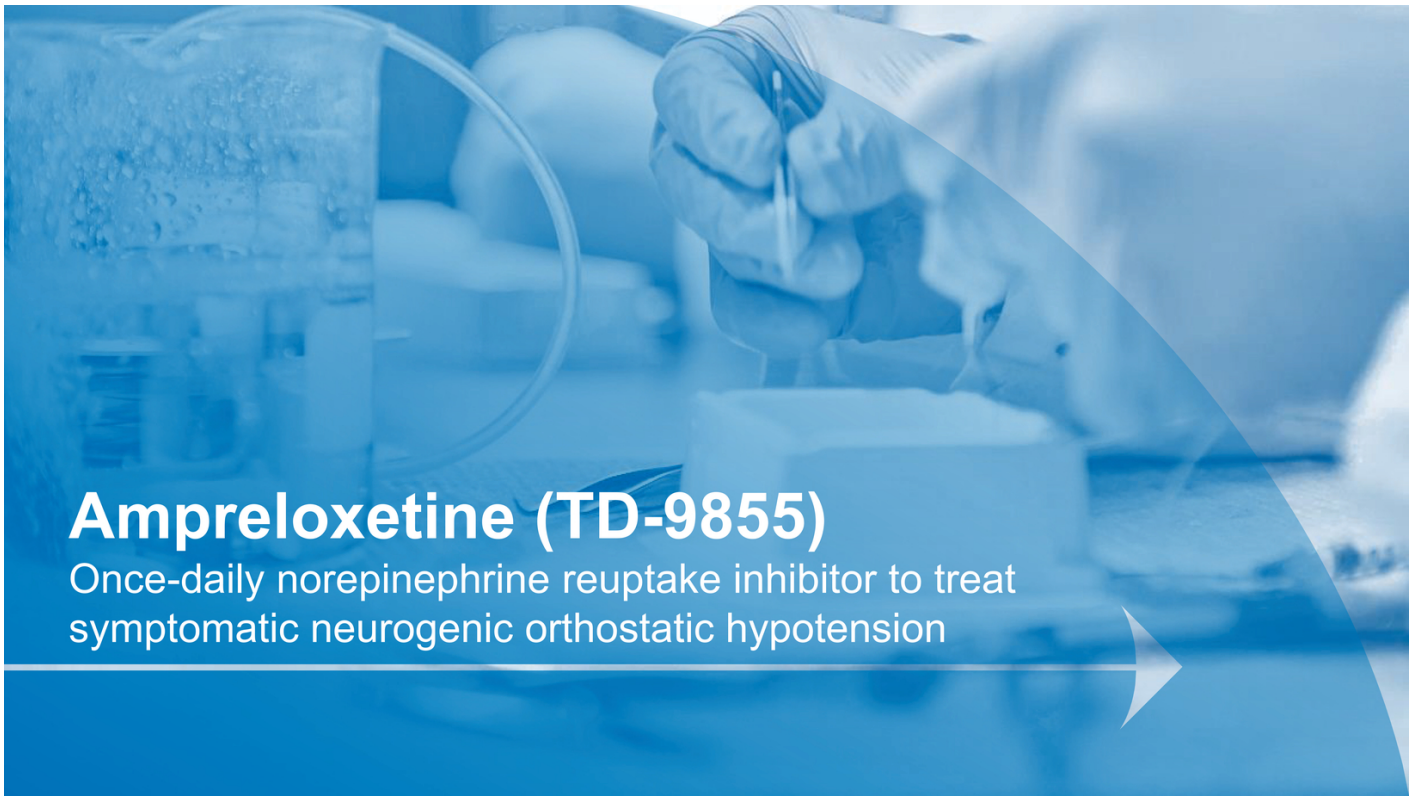
SEM, standard error of mean; S/F ratio, ratio of oxygen saturation in the blood vs the flow of oxygen administered to the patient.

Nezulcitinib 3 mg reduces relevant systemic biomarkers



https://www.medrxiv.org/content/10.1101/2021.03.09.21252944v1

BL, baseline; CI, confidence interval; CRP, C-reactive protein; GM, geometric mean; IL, interleukin; RAGE, receptor for advanced glycation end-products.



Ampreloxetine (TD-9855)

Once-daily norepinephrine reuptake inhibitor to treat symptomatic neurogenic orthostatic hypotension

Reduced quality of life, significant caregiver burden and limited therapeutic options for symptomatic nOH patients

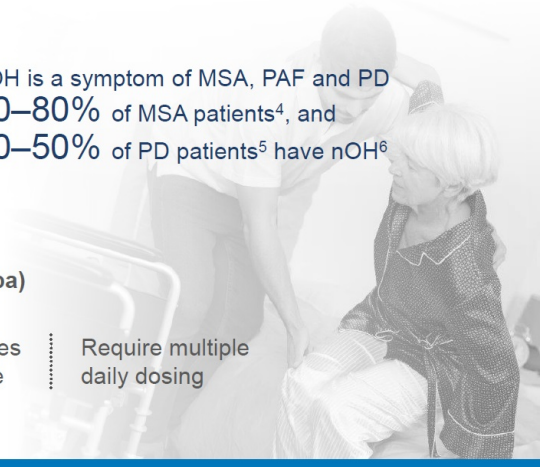
PATIENT POPULATION

~350K US patients[1]

~700K APAC patients[2]

~700K EU patients[3]

nOH is a symptom of MSA, PAF and PD
70–80% of MSA patients[4], and
30–50% of PD patients[5] have nOH[6]



CURRENT TREATMENT LANDSCAPE

Current treatments (midodrine, fludrocortisone, droxidopa) have significant limitations

- Subset of patients do not respond
- None demonstrate durable effect
- Safety profiles that limit use
- Require multiple daily dosing

STRATEGIC OPPORTUNITY

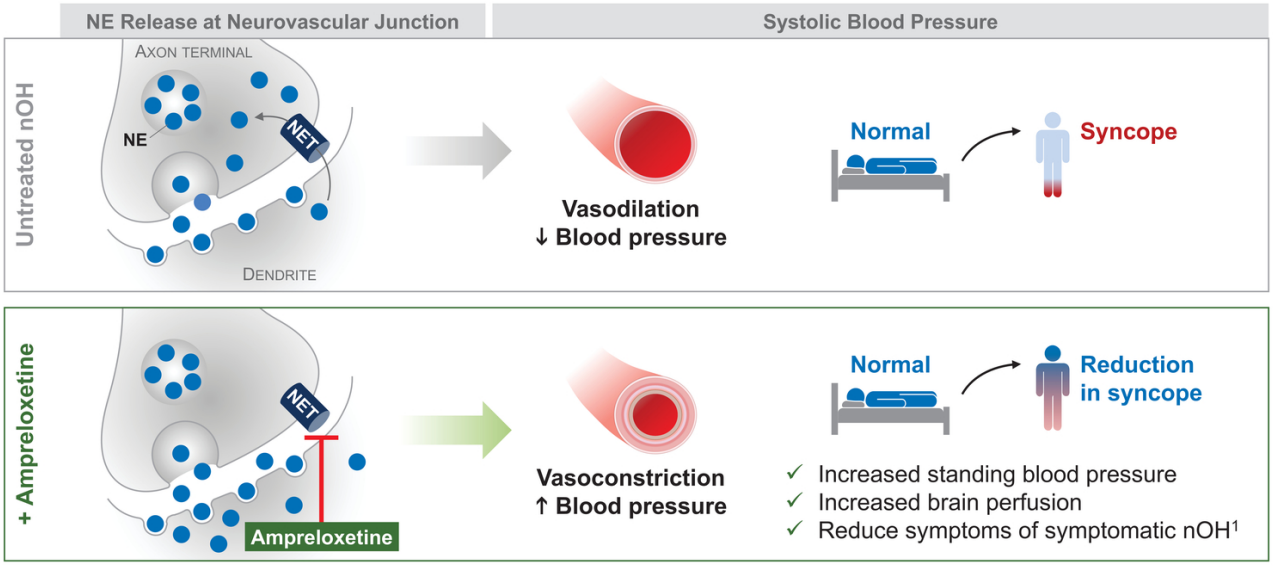
Ampreloxetine

Designed to reduce symptoms of nOH by prolonging the effect of endogenous norepinephrine with the potential to provide a meaningful and durable symptom improvement to underserved patients

Theravance Biopharma
Medicines That Make a Difference

1. https://www.parkinson.org/Understanding-Parkinsons/Statistics; https://www.ninds.nih.gov/Disorders/Patient-Caregiver-Education/Fact-Sheets/Multiple-System-Atrophy.
2. IQVIA Research 3. https://www.sciencedirect.com/science/article/abs/pii/S0924977X05000702; https://emedicine.medscape.com/article/1154583-overview#a6; Vanacore N, Bonifati V, Fabbrini G, Colosimo C, De Michele G, Marconi R, et al. Epidemiology of multiple system atrophy. ESGAP Consortium. European Study Group on Atypical Parkinsonisms. Neurol Sci. 2001 Feb. 22(1):97-9. [Medline]. 4. Mathias C, et al. J Neurol 1999;246:893-8. 5. Ha AD, et al. Parkinsonism Relat Disord 2011;17:625-8. 6. Not all patients are treated with prescription medication.
APAC, Asian and Pacific; MSA, multiple system atrophy; PAF, pure autonomic failure; PD, Parkinson's Disease; nOH, neurogenic orthostatic hypotension.

Designed to reduce symptoms of nOH by prolonging the effect of endogenous norepinephrine



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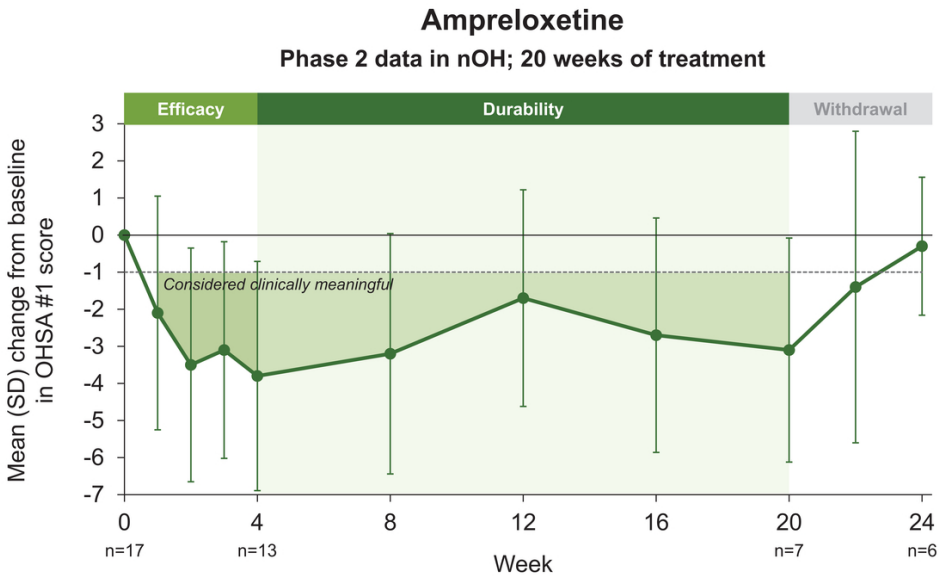
Medicines That Make a Difference

Palma JA, Kaufmann H. Mov Disord Clin Pract 2017;4:298-308.
NE, norepinephrine; NET, norepinephrine transporters; nOH, neurogenic orthostatic hypotension.

Ampreloxetine: Potential to provide meaningful and durable symptom improvement to underserved patients



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Medicines That Make a Difference

Baseline OHSA #1 (Orthostatic Hypotension Symptom Assessment Question 1) >4 points.
Negative change indicates improvement in symptoms; improvement of 1 point is defined as the MCID (minimal clinically important difference).
nOH, neurogenic orthostatic hypotension; SD, standard deviation.

Ampreloxetine: Phase 3 registrational program
Randomized, double-blind, placebo-controlled study

Study 0169

Key inclusion criteria: Age >30 y with symptomatic nOH with OHSA #1 score ≥4

Countries: Australia, Canada, Europe, New Zealand, Russia, UK, US

N=188
Randomization

Ampreloxetine

Placebo

Once-daily 10 mg oral dose:
4 weeks

Q3'21
Efficacy Data

Objectives

- **Primary:** Change from baseline in OHSA #1 score at Week 4*
- **Secondary:**
  - Change from baseline in OHSA composite score over 4 wk
  - Change from baseline in OHDAS composite score over 4 wk
  - PGI-C at Week 4
  - Incidence of falls

Status

- Phase 3 registrational program ongoing
- All participants who complete Study 0169 are eligible for Study 0170

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Medicines That Make a Difference

Note: Ampreloxetine Phase 3 registrational program is comprised of Studies 0169 and 0170; Study 171 safety data through week 26 will be included
*Orthostatic Hypotension Symptom Assessment Question 1: negative change indicates improvement in symptoms; improvement of 1 point is defined as the MCID (minimal clinically important difference).
Discontinuation rates for the Phase 3 trials as of Jan. 2020: 0169 – 5.3%.
nOH, neurogenic orthostatic hypotension; OHDAS, orthostatic hypotension daily activities scale; OHSA, Orthostatic hypotension symptom assessment; PGI-C, patient global impression of change. NCT03750552

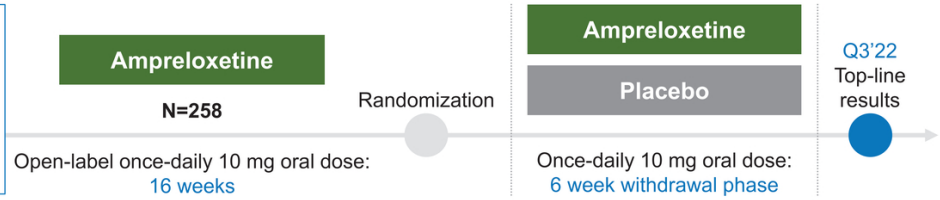
Ampreloxetine: Phase 3 registrational program
Placebo-controlled, randomized withdrawal study

REDWOOD Study 0170

An ampreloxetine study for nOH

Key inclusion criteria: Age >30 y with symptomatic nOH with OHSA #1 score ≥4

Countries: Argentina, Australia, Canada, Europe, New Zealand, Russia, UK, US



Objectives

- **Primary:** 1-pt worsening from baseline in both OHSA #1 score* and PGI-S during withdrawal phase
- **Secondary:** Changes from baseline at Week 6 post-randomization
  - OHSA #1
  - OHSA composite score
  - OHDAS composite score
  - PGI-S
  - % Time spent standing
  - Average no. of steps taken

Status

- Phase 3 registrational program ongoing
- All participants who complete Study 0170 are eligible for Extension Study 0171

*Negative change indicates improvement in symptoms; improvement of 1 point is defined as the MCID (minimal clinically important difference).
Discontinuation rates for the Phase 3 trials as of Jan. 2020: 0170 – 33.3%.
NCT03829657
nOH, neurogenic orthostatic hypotension; OHSA, orthostatic hypotension symptom assessment; PGI-S, patient global impression of disease severity.

Ampreloxetine: Phase 3 registrational program
6-month safety study + 3-year optional extension

Study 0171

Key inclusion criteria: patients who completed Study 0170 and, in investigator's opinion, would benefit from long-term treatment with ampreloxetine

Countries: Argentina, Australia, Canada, Europe, New Zealand, Russia, UK, US

Ampreloxetine

Once-daily oral dose: 182 weeks

Q3'22
Top-line results*

Primary endpoints

- Through Week 26:
  - Physical and neurological exams
  - Vital signs
  - ECGs
  - Clinical laboratory tests
  - Concomitant medications
  - AEs
  - Treatment compliance
  - Incidence of falls
  - Changes from baseline in C-SSRS

Status

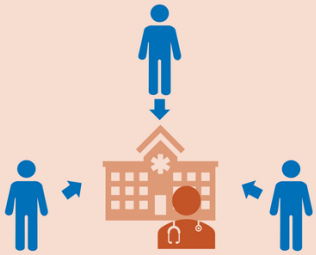
- Includes patients who completed Study 0170

*Through week 26; for FDA filing
NCT04095793
AE, adverse event; C-SSRS, Columbia Suicide Severity Rating Scale; ECG, electrocardiogram.

Decentralized trials move activities from the clinic to home

Global clinical trials are being decentralized along a continuum

Traditional Trial Operations



- Site-centric operating model
- Burden on site resources
- Patient burden

Decentralized Trial

- Patient-centric model
- Leverage technology for remote visits, monitoring and data collection
- Established home health and distribution channels

Source: Theravance Biopharma Clinical Operations.

Ampreloxetine: has the potential to transform Theravance Biopharma into an independent commercial biopharma

Established disease, targeted market

Established nOH treatment paradigm

nOH is included in medical treatment guidelines for PD and MSA patients; once diagnosed, patients get on drug treatment quickly

Specialist networks in place

A concentrated group of neurologists and cardiologists treat patients with nOH; 'at risk' patients already identified and managed by specialty institutions

An urgency to treat

Physicians report high urgency to treat snOH due to the high impact on patients' QoL, high risk of injury from falls and caregiver burden

A strong value proposition

Manageable opportunity

TBPH's infrastructure capable of commercializing ampreloxetine in the US with limited and targeted additions to current resources

Understanding of current access barriers

Meaningful value proposition will drive patient access; Ampreloxetine has the potential to improve the durability of treatment effect and thereby reduce costly events associated with nOH

Established patient advocacy

Strong message from PD and MSA advocacy groups that patients need new therapies to better manage nOH

MSA, multiple system atrophy; PD, Parkinson's disease; QoL, quality of life; snOH, symptomatic neurogenic orthostatic hypotension.

Izencitinib (TD-1473/JNJ-8398)

Oral gut-selective pan-JAK inhibitor to treat inflammatory bowel diseases

Need for new medicines to treat inflammatory bowel disease

PATIENT POPULATION

6.8M global cases, 2017[1]

1.6M current US patients[2]

Current US patients **780K** CD cases[3] **907K** UC cases[4]

$16B global IBD treatment market, 2018[5]

$31B US disease burden[2]

CURRENT TREATMENT LANDSCAPE

Standard of care:
Biologics have become the mainstay of treatment in moderate-to-severe patients

Steroids, immunosuppressants, and TNF inhibitors associated with side effects that further decrease HRQoL

STRATEGIC OPPORTUNITY

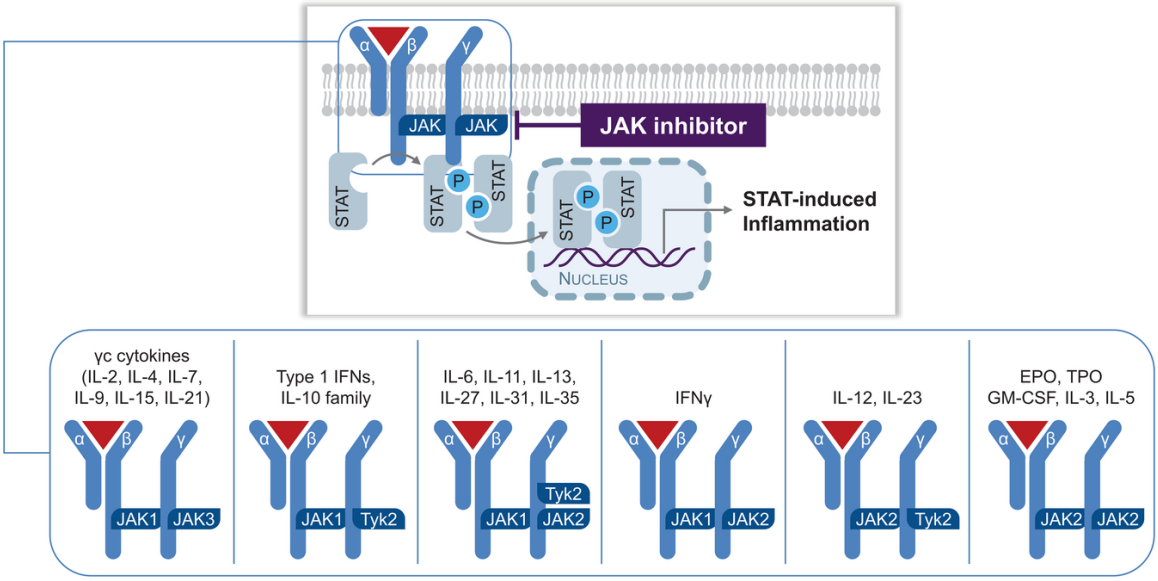
Izencitinib

Gut-selective agent: if used earlier in the course of disease, has potential to be a new cost-effective therapy option that reduces associated disease management costs and improves patient HRQoL

Theravance Biopharma
Medicines That Make a Difference

1. GBD 2017 Inflammatory Bowel Disease Collaborators. Lancet 2020;5:17-30. 2. https://www.crohnscolitisfoundation.org/sites/default/files/2019-02/Updated%20IBD%20Factbook.pdf.
3. https://www.healthline.com/health/crohns-disease/facts-statistics-infographic 4. https://med.stanford.edu/news/all-news/2020/02/stanford-scientists-link-ulcerative-colitis-to-missing-gut-micro.html
5. https://www.transparencymarketresearch.com/inflammatory-bowel-disease.html
CD, Crohn's disease; HRQoL, health-related quality of life; IBD, inflammatory bowel disease; TNF, tumor necrosis factor; UC, ulcerative colitis.

JAK-STAT pathway: orchestrating signaling of multiple pro-inflammatory cytokines



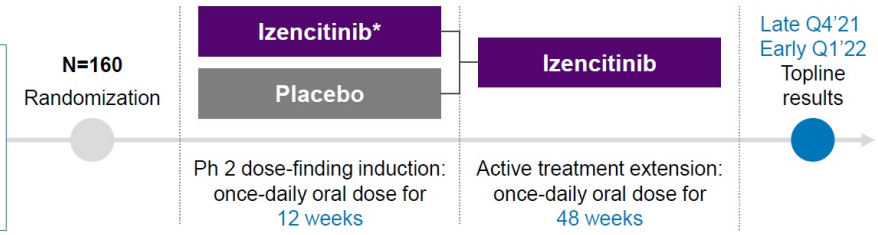
Clark JD, et al. J Med Chem 2014; 57:5023-5038.
EPO, erythropoietin; GM-CSF, granulocyte-macrophage colony-stimulating factor; IFN, interferon; IL, interleukin; JAK, Janus kinase; STAT, signal transducer and activator of transcription; TPO, thrombopoietin; Tyk, tyrosine kinase.

Izencitinib: Phase 2 study in Crohn's disease

DIONE STUDY Study 0173

Key inclusion criteria: Age ≥18 y with moderately-to-severely active CD (CDAI 220–450) with corticosteroid dependence or failure of conventional or biologic therapy

Countries: Africa, Asia, Australia, EU, Middle East, New Zealand, UK, USA



Endpoints

- **Primary:** Improvement in CDAI score at week 12 in patients with moderately to severely active CD
- **Exploratory:**
  - Clinical response measured by CDAI at 12 weeks
  - CDAI clinical remission at 12 weeks
  - SES-CD change from baseline to Week 12
  - Endoscopic response [Time Frame: 12 weeks]
  - SFAP clinical remission [Time Frame: 12 weeks]

Status

- Ongoing

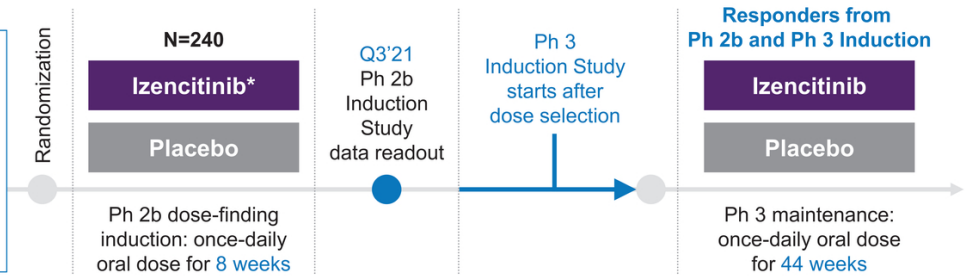
*2 izencitinib doses.
NCT03635112
CD, Crohn's disease; CDAI, Crohn's Disease Activity Index; SES-CD, Simple Endoscopic Score for Crohn's Disease; SFAP, Stool Frequency and Abdominal Pain.

Izencitinib: Phase 2b Induction study in ulcerative colitis

RHEA PROGRAM Study 0157

Key inclusion criteria: Age ≥18 y with moderately-to-severely active UC with corticosteroid dependence or failure of conventional or biologic therapy

Countries: Africa, Asia, Australia, EU, Middle East, North America, Japan



Endpoints

- **Primary:**
  - Change from baseline in tMS at Week 8
- **Secondary:**
  - Clinical remission by aMS components

Status

- Ph 3 Maintenance ongoing

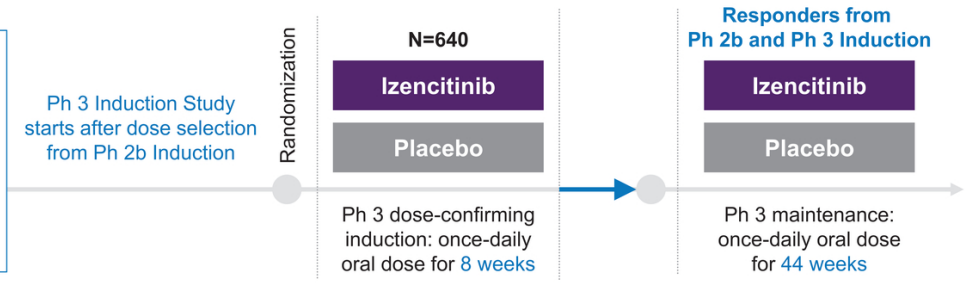
*3 izencitinib doses.
NCT03758443
aMS, adapted Mayo Score; tMS, total Mayo Score; UC, ulcerative colitis.

Izencitinib: Phase 3 studies in ulcerative colitis

RHEA PROGRAM Study 0157

Key inclusion criteria: Age ≥18 y with moderately-to-severely active UC with corticosteroid dependence or failure of conventional or biologic therapy

Countries: Africa, Asia, Australia, EU, Middle East, North America, Japan



Endpoints

- **Primary:**
  - Induction & Maintenance: clinical remission by aMS components at Week 8 and mWeek 44
- **Secondary:**
  - Induction & Maintenance: endoscopic healing, symptomatic remission, clinical response by aMS, mucosal healing, maintenance of clinical response, corticosteroid-free remission, maintenance of clinical remission

Status

- Phase 3 Induction study to begin post Phase 2b completion
- Phase 3 Maintenance study ongoing

NCT03758443

aMS, adapted Mayo Score; mWeek, maintenance Week; UC, ulcerative colitis.

Izencitinib: Phase 3 study in ulcerative colitis

RHEA PROGRAM Study 0164

Key inclusion criteria: Eligible patients from Ph 3 Maintenance Study of Protocol 0157

Countries: Africa, Asia, Australia, EU, Middle East, North America, Japan

Izencitinib

Long-term treatment
156 weeks (3 years)

Endpoints

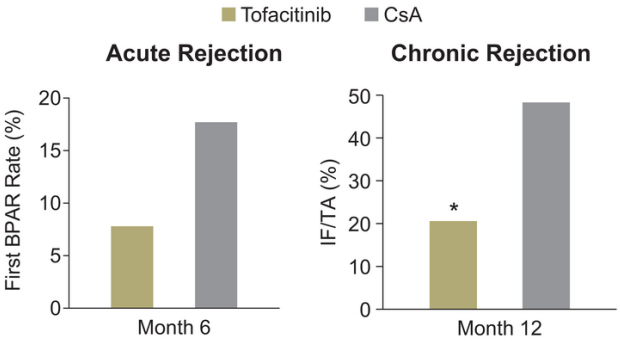
- **Primary:**
  - Assess the safety and tolerability of izencitinib administered for up to 3 years in patients with moderate-to-severe UC after participation in the Protocol 0157 Maintenance Study

NCT03758443
UC, ulcerative colitis.

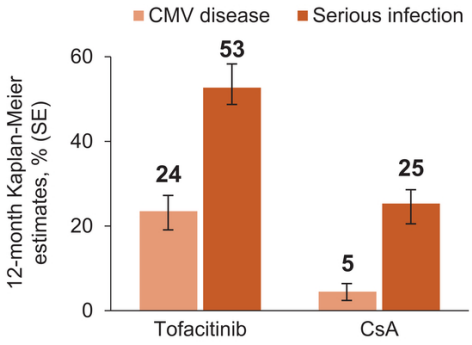
Pan-JAK inhibitors can prevent transplant rejections

Noninferiority trial of tofacitinib vs cyclosporine (CsA) in kidney transplant recipients[1]

Tofacitinib is superior to CsA in efficacy measures



Increased infection risk with tofacitinib over CsA



- JAK inhibition was superior to cyclosporine in prevention of acute and chronic rejections
- Serious infections increased with systemic JAK inhibitors including CMV

Theravance Biopharma
Medicines That Make a Difference

1. Vincenti F, et al. Am J Transplant 2015;15:1644-53.
*p<0.001 vs CsA.
BPAR, biopsy-proven acute rejection; CMV, cytomegalovirus; IF/TA, interstitial fibrosis/tabular atrophy; JAK, Janus kinase; SE, standard error; TWC2, time-weighted 2-h post-dose concentrations.

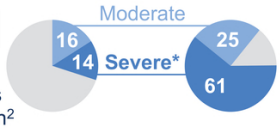

TD-8236
Potential first inhaled JAKi for asthma

High medical and economic burden in uncontrolled asthma

PATIENT POPULATION

339M cases worldwide[1]

25M US cases
8% of adults
8% of children[2]



Healthcare utilization[3]

~$58B US medical costs[4]

~$15B US asthma market (October 2020)[5]

CURRENT TREATMENT LANDSCAPE

ICS + LABA (often fail to control disease)

Approved biologics (affect subsets of patients)

- XOLAIR (omalizumab)
- NUCALA (mepolizumab)
- CINQAIR (reslizumab)
- FASENRA (benralizumab)
- DUPIXENT (dupilumab)

Step-up for severe asthma: LTRAs, tiotropium, OCS, biologics

JAK/STAT cytokines implicated in moderate-to-severe asthma

T2-high	T2-low
IL-4	**IL-23**/IL-12
IL-13	**IL-6**
IL-5	IL-27
TSLP	IFN-γ

Bold: biologics in development or approved.

STRATEGIC OPPORTUNITY

TD-8236

Potential to transform the treatment of respiratory inflammation by treating moderate-to-severe asthma regardless of T2 phenotype, including patients who remain symptomatic despite compliance on high-dose ICS

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Medicines That Make a Difference

*Asthma that requires high-dosage ICS + LABAs to prevent the disease from being uncontrolled) or asthma that remains uncontrolled despite treatment.

1. World Health Organization; 2. https://www.aafa.org/asthma-facts/; 3. Sadatsafavi, M., et al. Can Respir J 2010;17:74-80. 4. Nurmagambetov T, et al. Ann Am Thorac Soc 2018;15:348-56; 5. TBPH estimate based on multiple data sources. ICS, inhaled corticosteroids; IFN, interferon; IL, interleukin; JAK, Janus kinase; LABA, long-acting β2 agonists; LTRA, leukotriene receptor antagonist; OCS, oral corticosteroid; STAT, signal transducer and activator of transcription; T2, type 2; TSLP, thymic stromal lymphopoietin.

TD-8236: Phase 1 clinical trial design

Parts A & B completed September 2019; Part C enrollment completed — data reported in Q4 2020

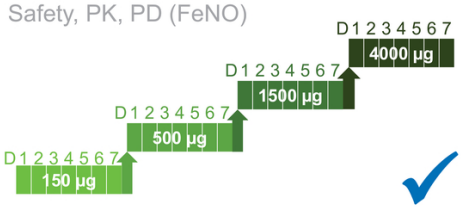
Part A: SAD (Healthy volunteers)

Safety, PK

All cohorts: N=6 active/2 Placebo

Part B: MAD (Mild asthmatics)

Safety, PK, PD (FeNO)

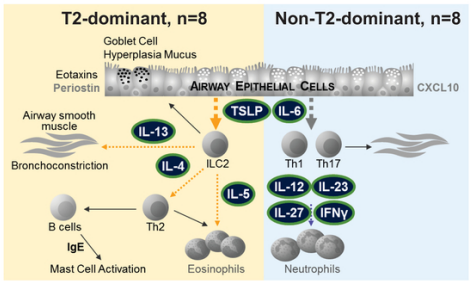


Part C: MoA Biomarkers

(Moderate-to-severe asthmatics + ICS)

N=16 active/8 placebo

D1 2 3 4 5 6 7 1500 µg



- Goal: build confidence in compound, MoA and dose in early-development
- **Endpoints: FeNO; pSTAT1 and pSTAT6 in bronchoalveolar lavage fluid; cytokines; epithelial gene expression**

Theravance Biopharma
Medicines That Make a Difference

CXCL, chemokine (C-X-C motif) ligand; FeNO, fractional exhaled nitric oxide; ICS, inhaled corticosteroids; IFN, interferon; IgE, immunoglobulin E; IL, interleukin; ILC2, type 2 innate lymphoid cells; MAD, multiple-ascending dose; MoA, Mechanism of Action; PK, pharmacokinetic; PD, pharmacodynamic; pSTAT, phosphorylated signal transducer and activator of transcription; SAD, single-ascending dose; T2, type 2; Th2, T helper type 2; TSLP, thymic stromal lymphopoietin.

TD-8236: Positive Phase 1 trial in healthy subjects and patients with mild and moderate-to-severe asthma

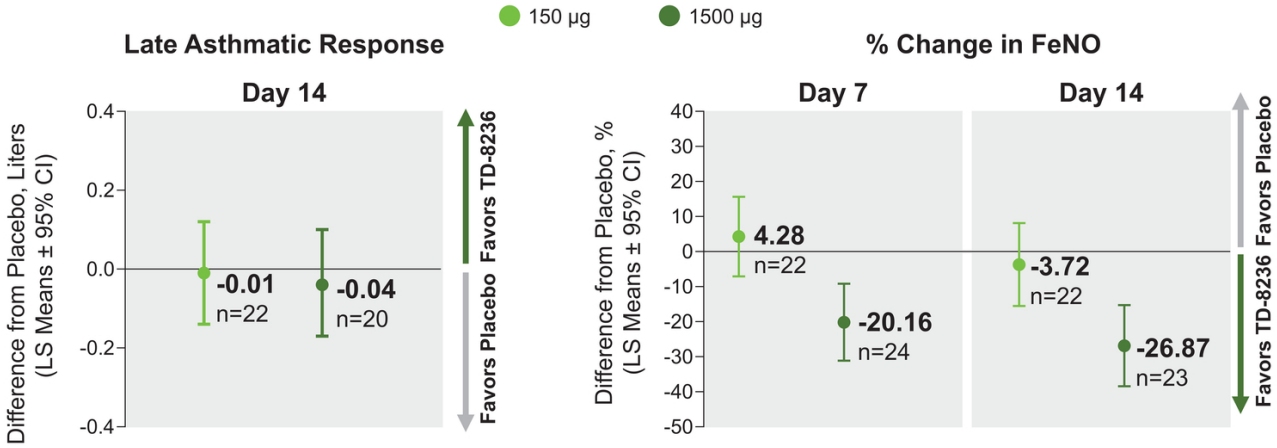
Phase 1 Profile	Healthy Volunteer Single Dose (Part A)	Mild Asthma Multiple Dose (Part B)	Moderate-to-Severe Asthma [+ ICS] Multiple Dose (Part C)
Generally well tolerated	✓	✓	✓
Minimal systemic exposure	✓	✓	✓
PK and PD profile consistent with once-daily dosing	✓	✓	✓
Biologic activity in lungs of patients with asthma		✓ ↓ FeNO	✓ ↓ FeNO, pSTAT1, pSTAT6

- Biomarkers of JAK target engagement (pSTAT1 and pSTAT6) significantly reduced in lungs of T2 high and T2 low moderate/severe asthmatics on top of ICS
- Ongoing analysis of effect of TD-8236 on additional biomarkers including cytokines and gene expression

FeNO, fractional exhaled nitric oxide; ICS, inhaled corticosteroids; JAK, Janus kinase; PK, pharmacokinetic; PD, pharmacodynamic; pSTAT, phosphorylated signal transducer and activator of transcription; T2, type 2.

No impact of TD-8236 on the Late Asthmatic Response (LAR)

Significant reductions in inflammation marker (FeNO) and favorable safety and tolerability



- TD-8236 was generally well tolerated as a single-daily dose administered for 14 consecutive days

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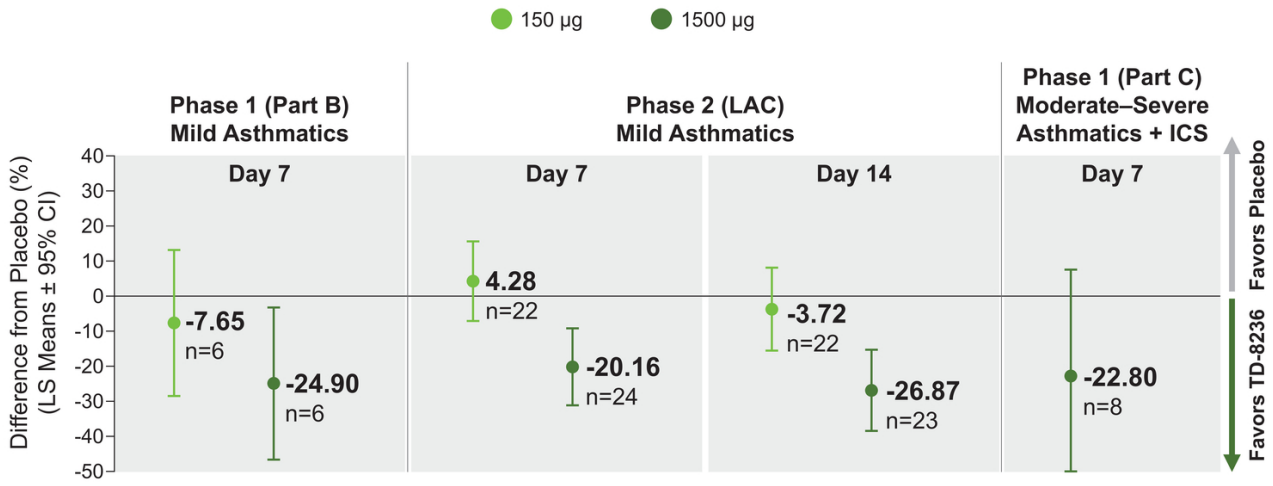
Primary Endpoint: Weighted Mean Area Under the Curve, 3–8 h.
CI, confidence interval; FeNO, fractional exhaled nitric oxide; LS, least-squares.

TD-8236 FeNO reductions consistent across Phase 1 and 2



- FeNO reductions observed in moderate-to-severe asthmatics taking inhaled corticosteroids

CI, confidence interval; FeNO, fractional exhaled nitric oxide; ICS, inhaled corticosteroids; LAC, lung allergen challenge; LS, least-squares.

TD-5202

Organ-gut selective irreversible JAK3 inhibitor
to treat inflammatory intestinal diseases

Celiac disease has no current treatments and serious health consequences

PATIENT POPULATION

1%
Global prevalence[1]

3.3M
US patients[2,3]

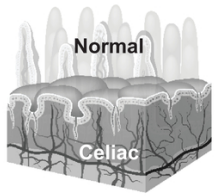
4–4.5x
increase in US over past 50 y[4]

>2x
higher healthcare costs than controls[5]

CURRENT TREATMENT LANDSCAPE

No approved treatment
Only available intervention is strict life-long gluten-free diet

30% of diagnosed patients are poorly controlled despite best dietary efforts[6]



STRATEGIC OPPORTUNITY

TD-5202

Organ-gut selective irreversible JAK3 inhibitor:
potential to deliver significant value for both patients and payers

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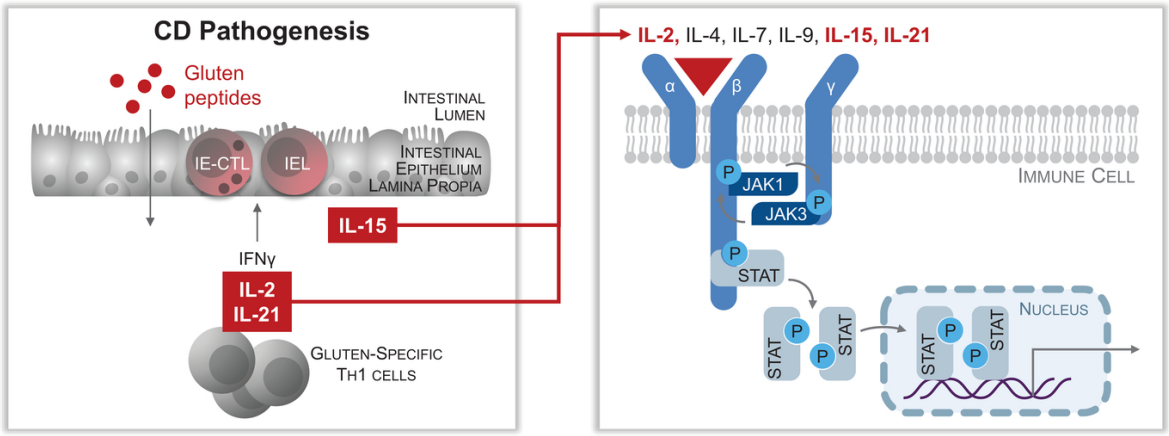
1. http://www.drschaer-institute.com/us/celiac-disease/epidemiology-1033.html; 2. 1% prevalence in US, BeyondCeliac.org; 3. 2018 US population 327M Census.gov.
4. Reunala T, et al. Nutrients 2018;10;pii: E602; 5. Guandalini et al. Digestive Diseases Sciences 2016;61:2823-30; 6. Theravance Market Research.
JAK, Janus kinase.

JAK3-dependent cytokines play central role in pathogenesis of celiac disease



- Proof-of-relevance from recent positive Phase 2 data with systemic JAK3 inhibitor in alopecia areata, another T-cell mediated disease
- Localized JAK3 inhibition has the potential to avoid systemic immunosuppression (genetic JAK3 deficiency leads to severe immunodeficiency)

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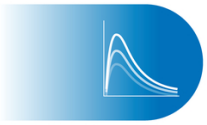
Figure adapted from Jabri B and Sollid L. J Immunol 2017;198:3005-14.
CD, Crohn's disease; IE-CTL, intraepithelial cytotoxic lymphocyte; IEL, intraepithelial lymphocyte; IFN, interferon; IL, interleukin; JAK, Janus kinase; STAT, signal transducer and activator of transcription; Th1, T helper 1 cells.

TD-5202 First-in-human overall results summary

TD-5202: generally well-tolerated (single dose ≤2000 mg, multiple doses ≤1000 mg BID) for 10 consecutive days in healthy subjects

- No serious or severe AEs were reported
- All treatment-emergent AEs in TD-5202-treated subjects were mild in severity

- No clinically significant changes from baseline in vital signs and ECG assessments
- No clinically significant changes in chemistry or hematology parameters
  - No changes in NK cell count



- Systemic exposures were dose proportional from 100 to 1000 mg BID
- Low steady-state systemic exposures: mean $C_{max,ss}$ ~11-fold below the protein-adjusted JAK IC_{50} at the highest tested dose (1000 mg BID), consistent with a gut-selective approach

AE, adverse event; BID, twice daily; $C_{max,ss}$, maximal steady-state concentration; ECG, electrocardiogram; IC_{50}, inhibitory concentration at which 50% of JAK signaling is blocked; JAK, Janus kinase; IC_{50}, NK, natural killer.

Inhaled ALK5i

Potential best-in-disease therapy for the treatment of idiopathic pulmonary fibrosis (IPF)

Idiopathic pulmonary fibrosis (IPF) remains a fatal chronic lung disease with limited treatment options

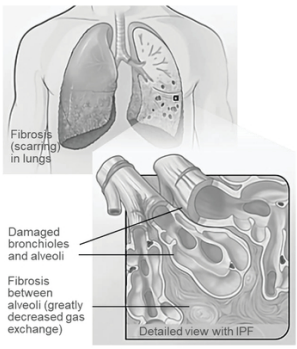
PATIENT POPULATION

140,000
US prevalence;
currently orphan disease[1,2]

Profound dyspnea, unrelenting cough, impairment of activities of daily living

Mortality with IPF remains high

Lungs with IPF[3]



CURRENT TREATMENT LANDSCAPE

Limited treatment options

2 currently approved therapies, with modest efficacy and poor tolerability

STRATEGIC OPPORTUNITY

Inhaled ALK5i

Potential first-in-class inhaled ALK5 inhibitor anti-fibrotic agent for IPF
Despite treatment with the current SoC, IPF patients continue to experience disease progression and exacerbation

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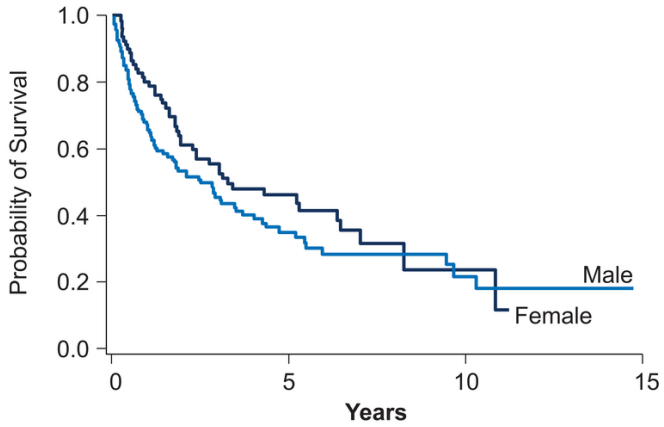
1. Raghu G, et al. Lancet Resp. 2014; 2(7):566-572; 2. Raghu G, et al. Eur Respir J. 2016: 48(1):179-186; 3. National Heart Lung and Blood Institute (NIH), Public Domain, https://commons.wikimedia.org/w/index.php?curid=29590103.
ALK5i, transforming growth factor β receptor I kinase inhibitor; Soc, Standard of Care.

Significant opportunity remains for effective IPF treatments



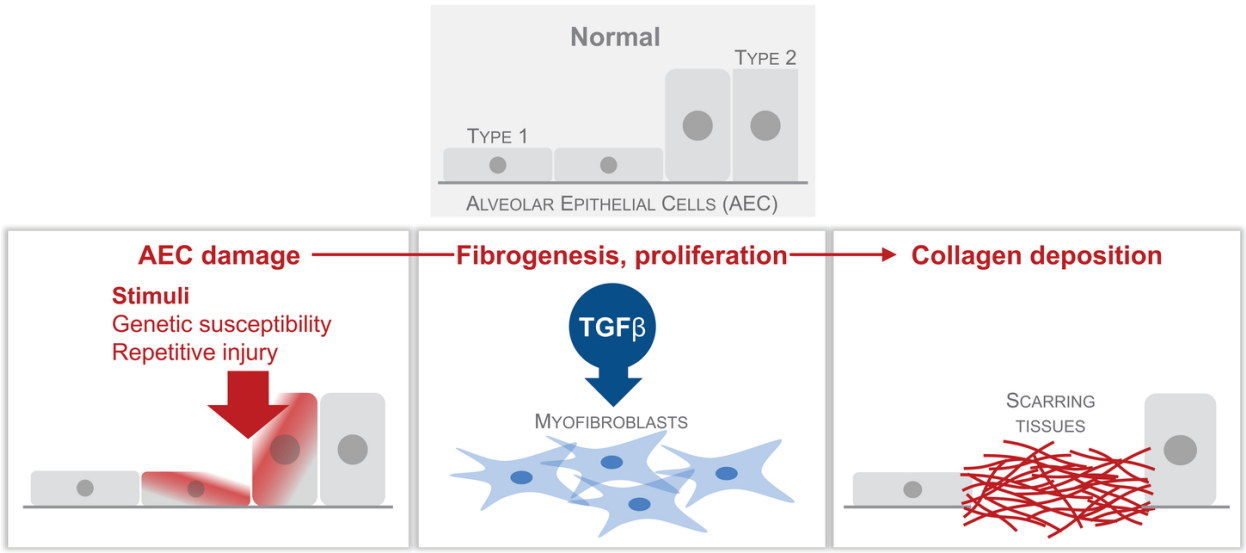
- Mortality with IPF remains high
  - <50% alive 3 years after diagnosis[1]

Goal To arrest disease progression with improved tolerability

1. King TE, et al. Am J Respir Crit Care Med 2001;164:1171-81.
IPF, idiopathic pulmonary fibrosis.

Targeting the TGFβ pathway

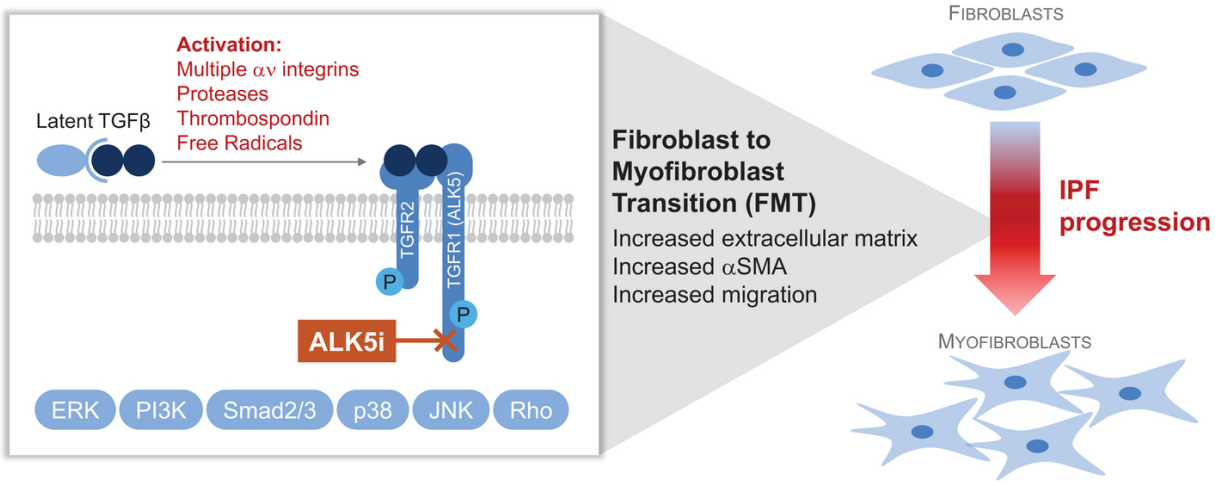
A core signaling pathway that drives fibrosis



TGFβ, transforming growth factor β.

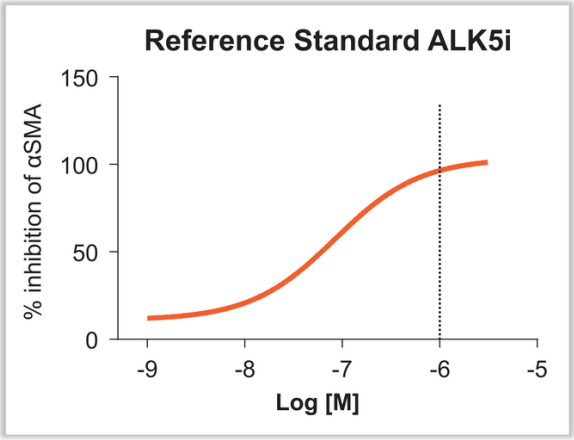
Selectively targeting the TGFβ pathway through ALK5 inhibition

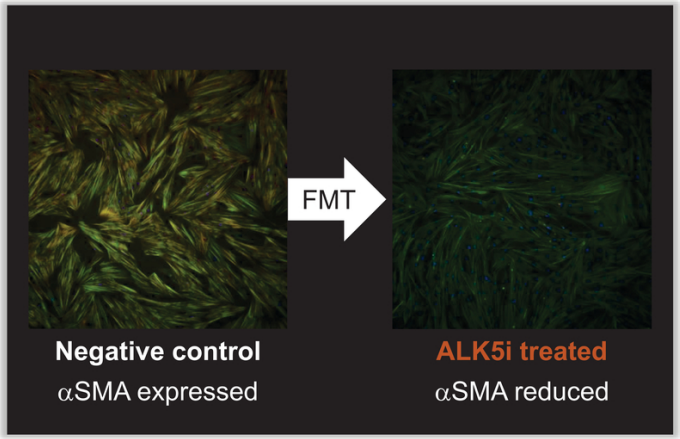
Inhibiting a core signaling pathway that drives fibrosis regardless of activation mechanism



Adapted from: Neuzillet C, et al. Oncotarget 2013;5:78–94.
αSMA, α-smooth muscle actin; ERK, extracellular signal-regulated kinase; IPF, idiopathic pulmonary fibrosis; JNK, c-Jun N-terminal kinase; PI3K, phosphatidylinositol-4,5-bisphosphate 3-kinase; Smad2/3, mothers against decapentaplegic homolog 2/3; TGFR (ALK5), transforming growth factor receptor.

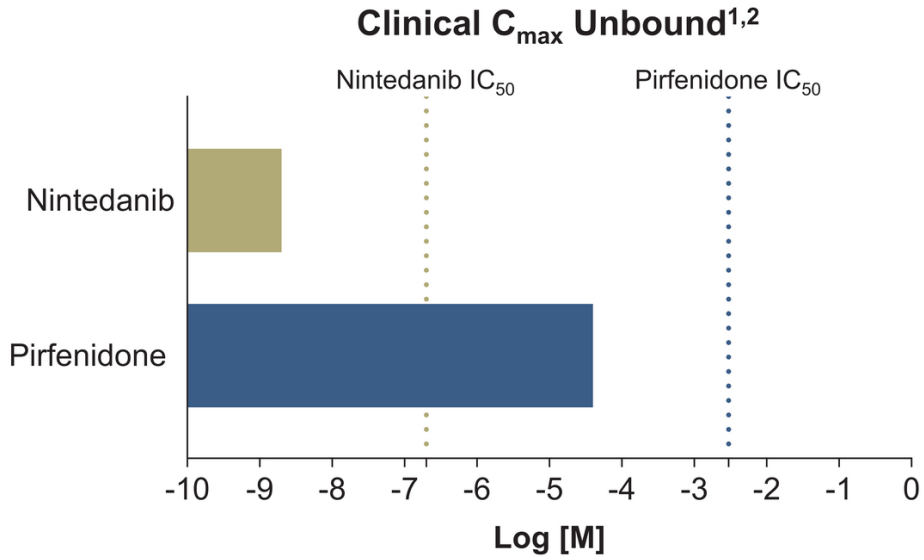
ALK5 inhibition directly interrupts FMT in IPF





ALK5i, transforming growth factor β receptor I kinase inhibitor; αSMA, α-smooth muscle actin; FMT, fibroblast to myofibroblast transition.

Current treatment options have no effect on FMT at clinically relevant concentrations

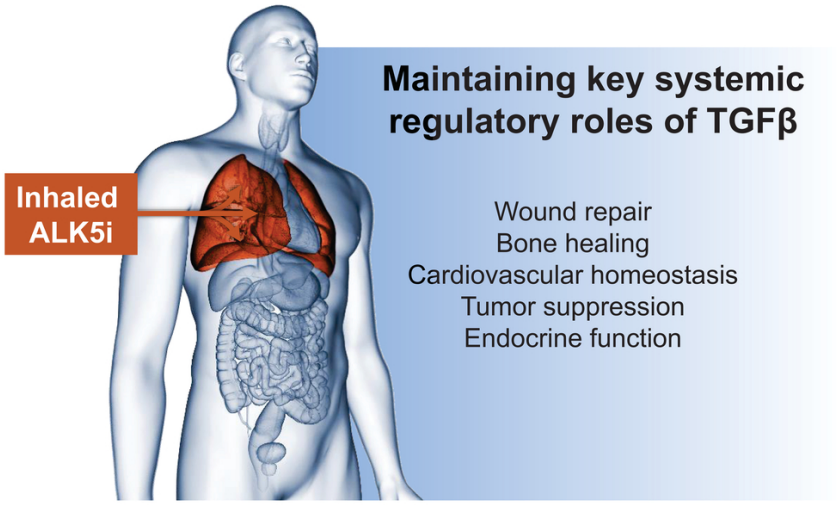


1. https://www.tga.gov.au/sites/default/files/auspar-nintedanib-esilate-160208.pdf.
2. Ogura T, et al. Eur Respir J. 2015;45:1382-92.

C_{max}, maximal concentration; FMT, fibroblast to myofibroblast transition; IC_{50}, half maximal inhibitory concentration.

Lung selectivity avoids unwanted systemic side effects

Minimizing systemic inhibition of a cytokine essential for homeostasis



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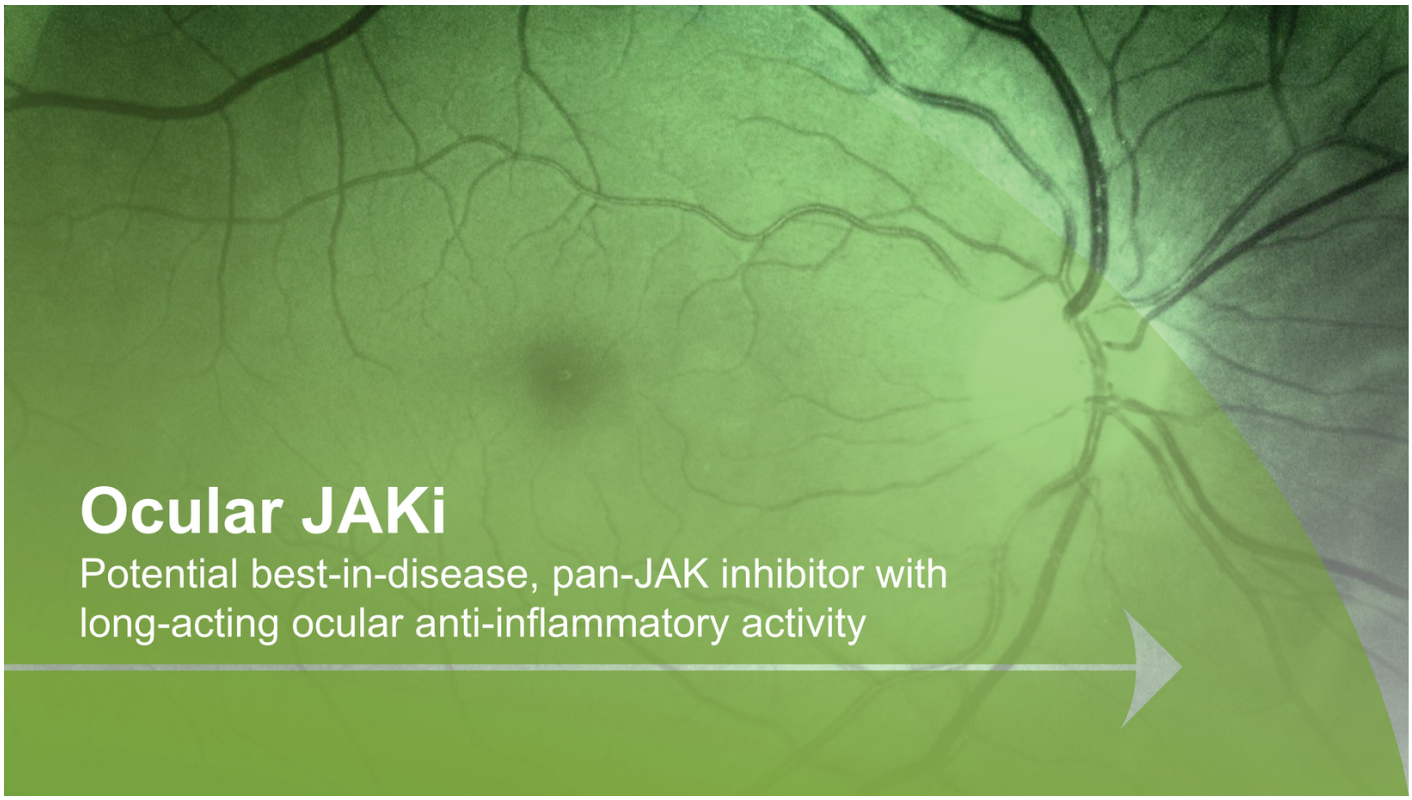
Modified from: Akhurst RJ, Hata A. Nat Rev Drug Discov 2012;11:790-811.
ALK5i, TGFβ receptor I kinase inhibitor; TGFβ, transforming growth factor β.



Ocular JAKi

Potential best-in-disease, pan-JAK inhibitor with long-acting ocular anti-inflammatory activity

Diabetic macular edema causes blindness in diabetics

PATIENT POPULATION

2.7 million US prevalence[1]

#1 cause of blindness in diabetes[2]

140% higher direct and indirect healthcare costs in patients with DME vs diabetics without ocular disease[3]

CURRENT TREATMENT LANDSCAPE

1st — **Anti-VEGF treatments** Most patients have suboptimal response

2nd — **Intraocular steroids** Side effects limit utility

Nonpharmacological treatments (e.g. laser coagulation) limited efficacy and significant adverse events

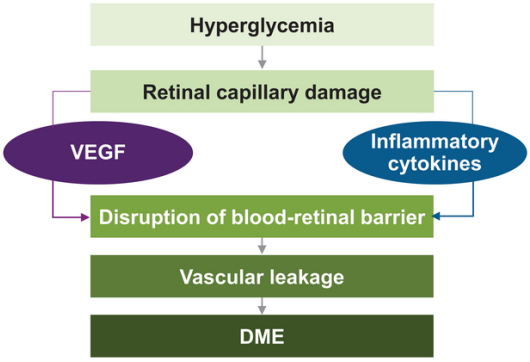
STRATEGIC OPPORTUNITY

Ocular JAKi

Potential to offer an alternative treatment for DME patients who are not optimally responding to treatment with VEGFi

2. Romero-Aroca, World J Diabetes 2011;2(6): 98-104. 3. Lee et al Curr Med Res Opin 2008;24:1549-59.
Images from Angiogenesis Foundation, www.scienceofdme.org.
DME, Diabetic macular edema; JAKi, Janus kinase inhibitor; VEGFi, vascular endothelial growth factor inhibitor.

Inflammation, not just VEGF, is a key driver of DME



Current Pharmacological Treatments

Intraocular anti-VEGF agents

- One third do not respond to anti-VEGF while another third have a suboptimal response[1]
- Require frequent intravitreal injections

Intraocular steroids

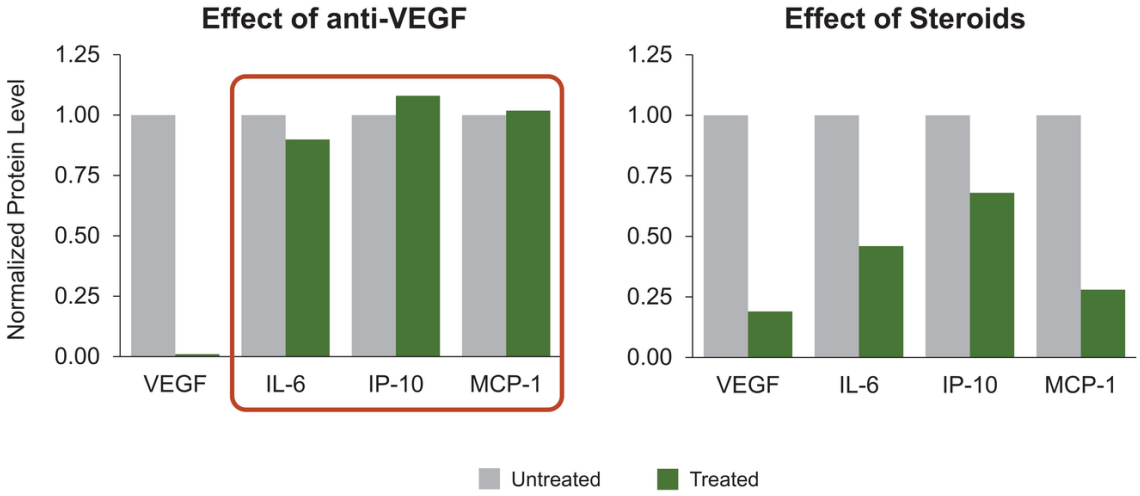
- High frequency of formation of cataracts and glaucoma

Need for broad, sustained release, anti-inflammatory with a safer side-effect profile

1. Gonzalez VH, et al. Am J Ophthalmol 2016;172:72-79.

DME, diabetic macular edema; VEGF, vascular endothelial growth factor.

Unmet need for an anti-inflammatory drug: opportunity for eye-selective JAK inhibition



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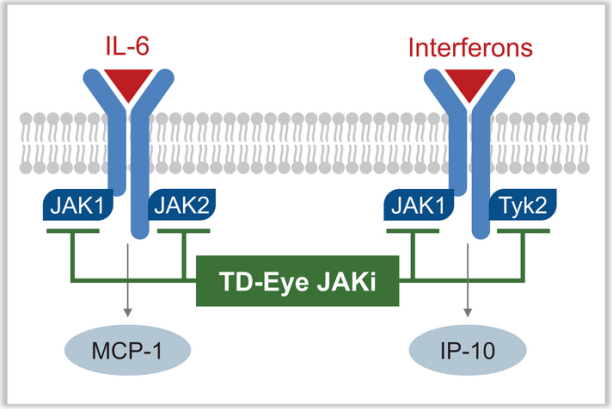
Adapted from Sohn HJ, et. al. Am J Ophthalmol 2011; 152:686-694.
IL-6, interleukin-6; IP-10, interferon γ-induced protein 10; JAK, Janus kinase; MCP-1, monocyte chemoattractant protein-1; VEGF, vascular endothelial growth factor.

Ocular pan-JAK inhibition has the potential to address key disease pathways in DME



TD-EyeJAKi inhibits key DME inflammatory pathways:

- IL-6 and interferon signaling pathways in human primary cells
- IL-6 induced pSTAT3 and interferon-induced IP-10 in the back of the eye *in vivo*

DME, diabetic macular edema; IL-6, interleukin-6; IP-10, interferon γ-induced protein 10; JAK, Janus kinase; MCP-1, monocyte chemoattractant protein-1; pSTAT, phosphorylated signal transducer and activator of transcription; Tyk, tyrosine kinase; VEGF, vascular endothelial growth factor.

A pan-JAK inhibitor designed for eye selectivity with projected dosing interval of at least three months