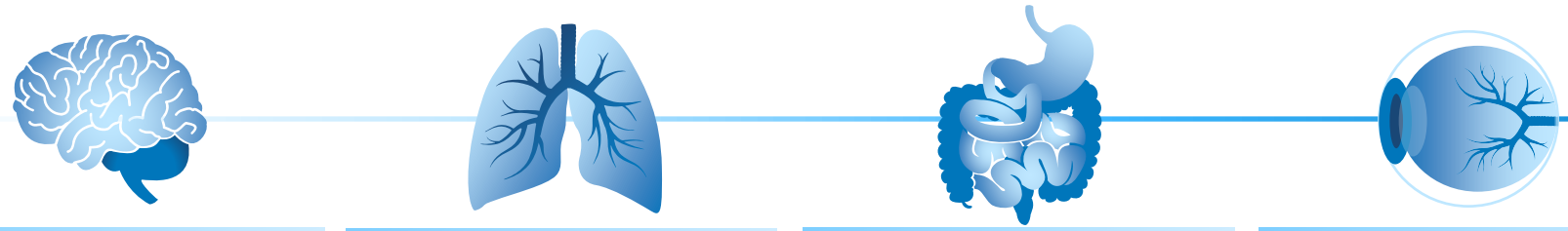
JP Morgan 2021
APPENDIX

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



Symptomatic nOH
(Neurogenic orthostatic hypotension)

COPD
(chronic obstructive pulmonary disorder) — APPROVED

Asthma

COVID-19

Lung Transplant Rejection

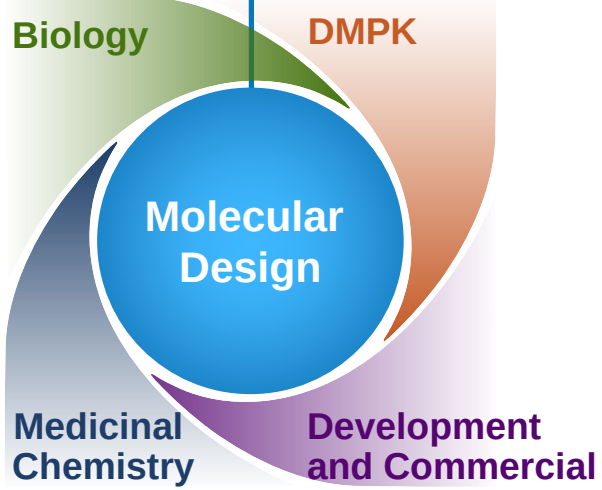
IPF (idiopathic pulmonary fibrosis)

CD
(Crohn's disease)

UC
(ulcerative colitis)

Celiac Disease

DME
(diabetic macular edema)



DMPK, drug metabolism and pharmacokinetics; GI, gastrointestinal.

YUPELRI® (revefenacin) inhalation solution

First and only once-daily, nebulized maintenance medicine for COPD

YUPELRI® launch metrics

Strong customer acceptance and market uptake

FORMULARY[1]

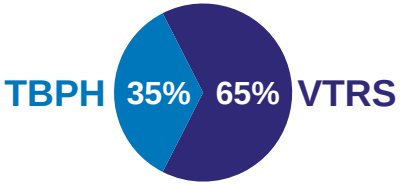
- **191 wins** (equates to 363 accounts)
- **78% of formulary accounts ordering**
- **100% medical support requests fulfilled** <30 days

PATIENT

- **Field force continues hybrid approach to customer interactions (live and virtual)**
- **~50,000 patients[2] prescribed** *(through Q3 2020)*

ACCESS

- **100% Medicare Part B[3]**
- **74% of commercial payer lives covered** (comprises **~8%** of the YUPELRI® business)



- **Theravance Biopharma's implied 35% share of Net Sales during Q3 2020 was $13M**
- **Increased market share and achieved quarter-over-quarter Net Sales growth of 22%**

Majority of YUPELRI® volume flows through durable medical equipment channel (approximately 3-month lag in data capture); remaining volume flows through hospitals, retail and long-term care pharmacies. Wholesale acquisition cost (WAC): $1,103 per month (or ~$37 per day). 1. Launch through October 2, 2020. 2. TBPH estimate derived from integrating multiple data sources. 3. For patients with supplemental insurance; approximately 20% of patients may be responsible for co-pay and/or supplemental insurance. Source: www.CMS.gov.

Key Success Drivers for YUPELRI®

Launch to Date

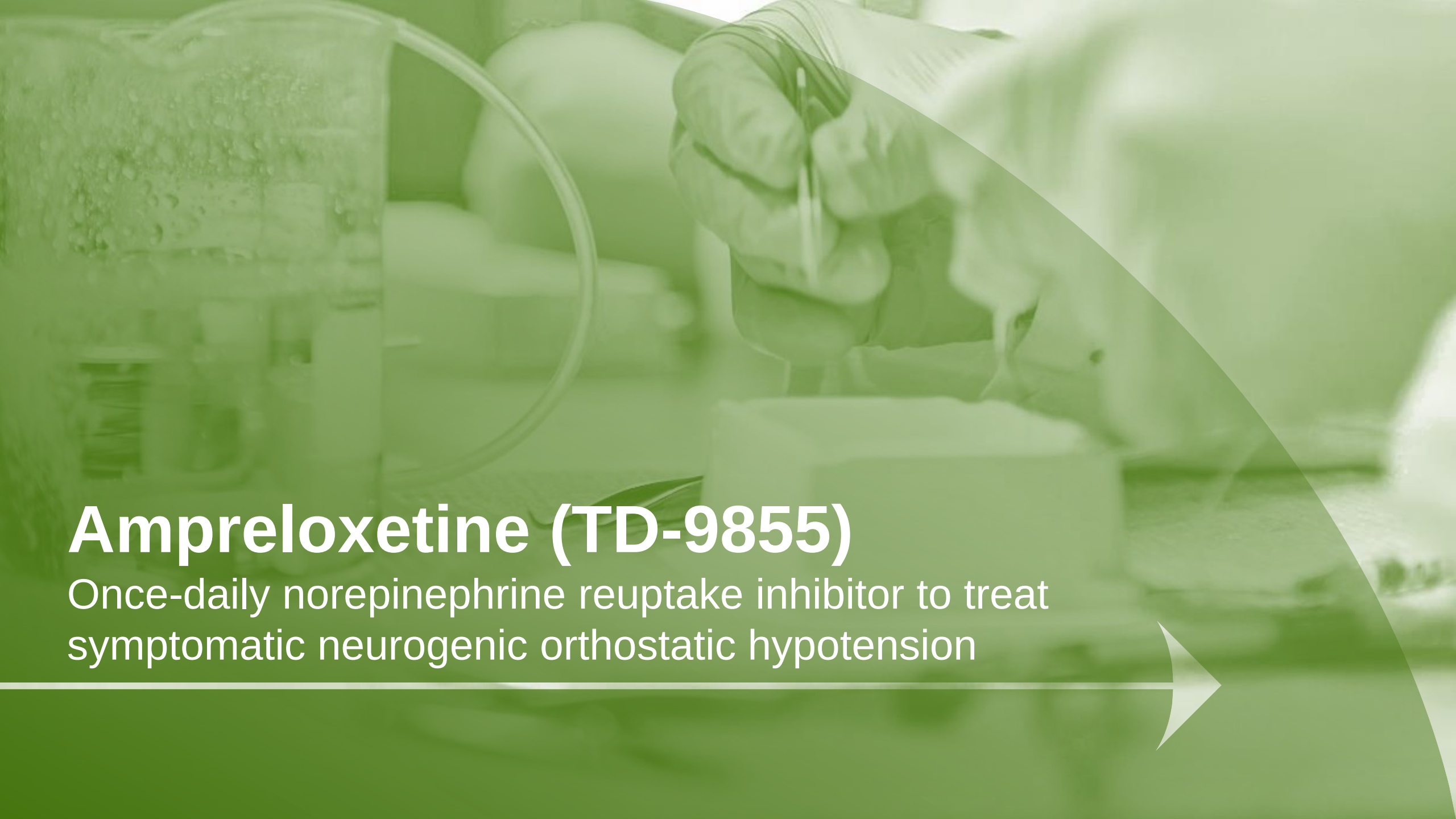
- Established Nebulized LAMA Market Leader
- Continued growth of hospital accounts with YUPELRI® on formulary
- Successful partnership with VIATRIS leading to continued growth in Community and overall brand
- Strong access with payers / Medicare Part B
- 18% higher refill rate over 12 months vs. Nebulized LABA average[1]

2021 and Beyond

- Expected growth of hospital account formularies as well as overall prescriber base
- Further communication of GOLD guidelines recognizing LAMAs as foundational therapy for the majority of patients with COPD, especially as Nebulized LABAs reach LOE
- Continued momentum with an alternative therapy to handhelds and short-acting agents used for maintenance therapy

YUPELRI revefenacin inhalation solution

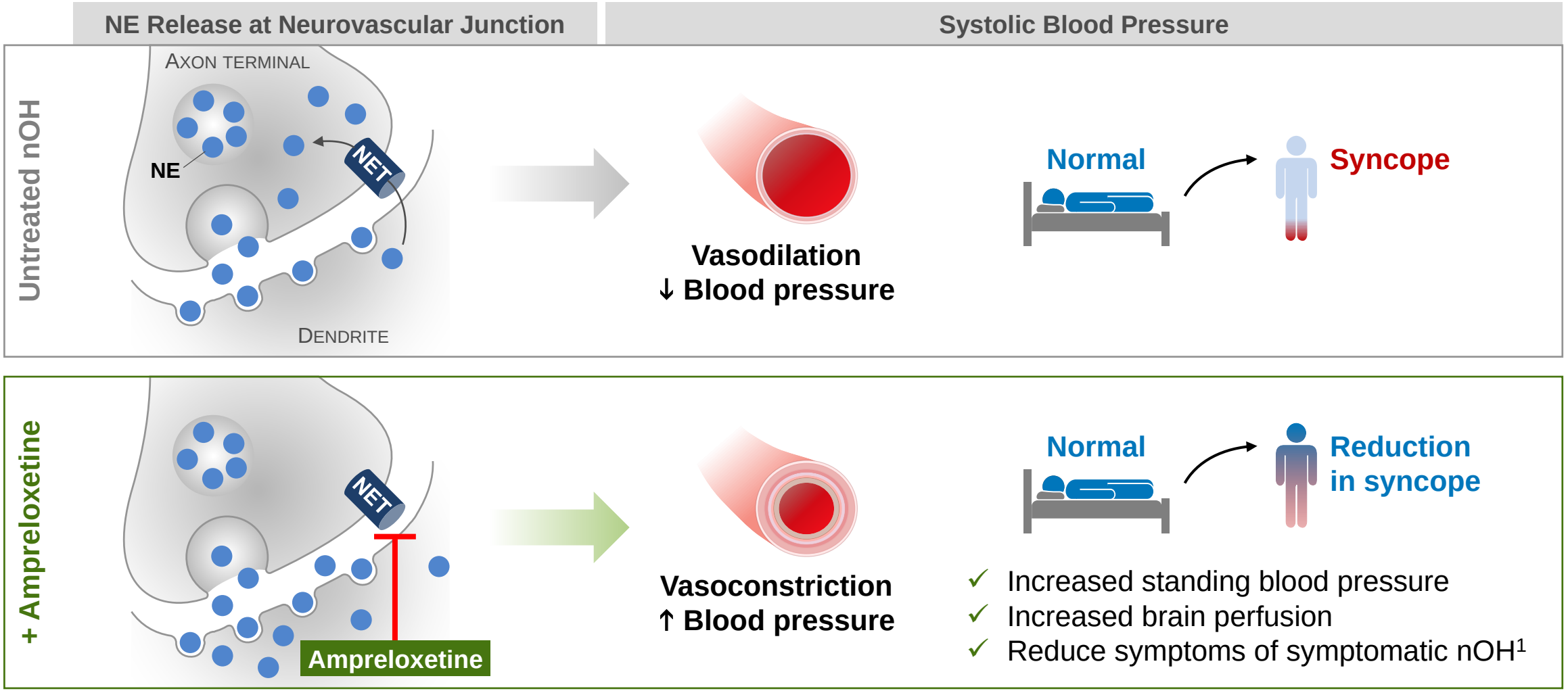
1. Symphony Health Patient-Level Claims Data through Q2'20.
LABA, long-acting beta agonist.; LAMA, long-acting muscarinic agonist



Ampreloxetine (TD-9855)

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

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

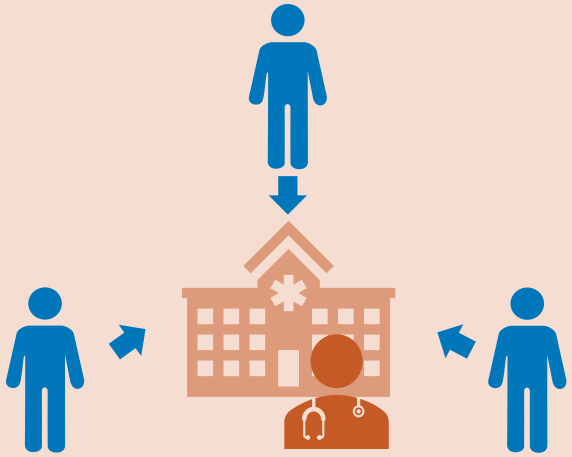


1. Palma JA, Kaufmann H. Mov Disord Clin Pract 2017;4:298-308.
NE, norepinephrine; NET, norepinephrine transporters.

Decentralized trials move activities from the clinic to home

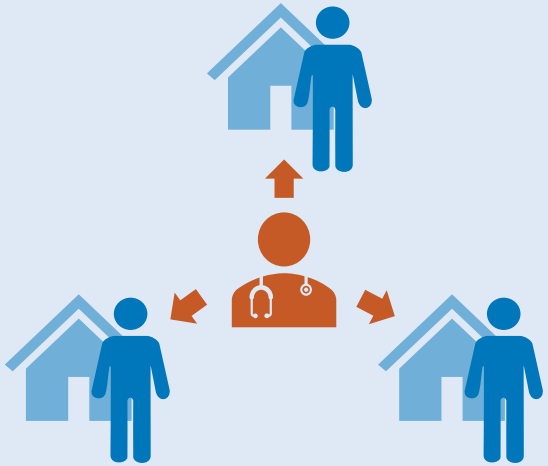
Global clinical trials are being decentralized along a continuum

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

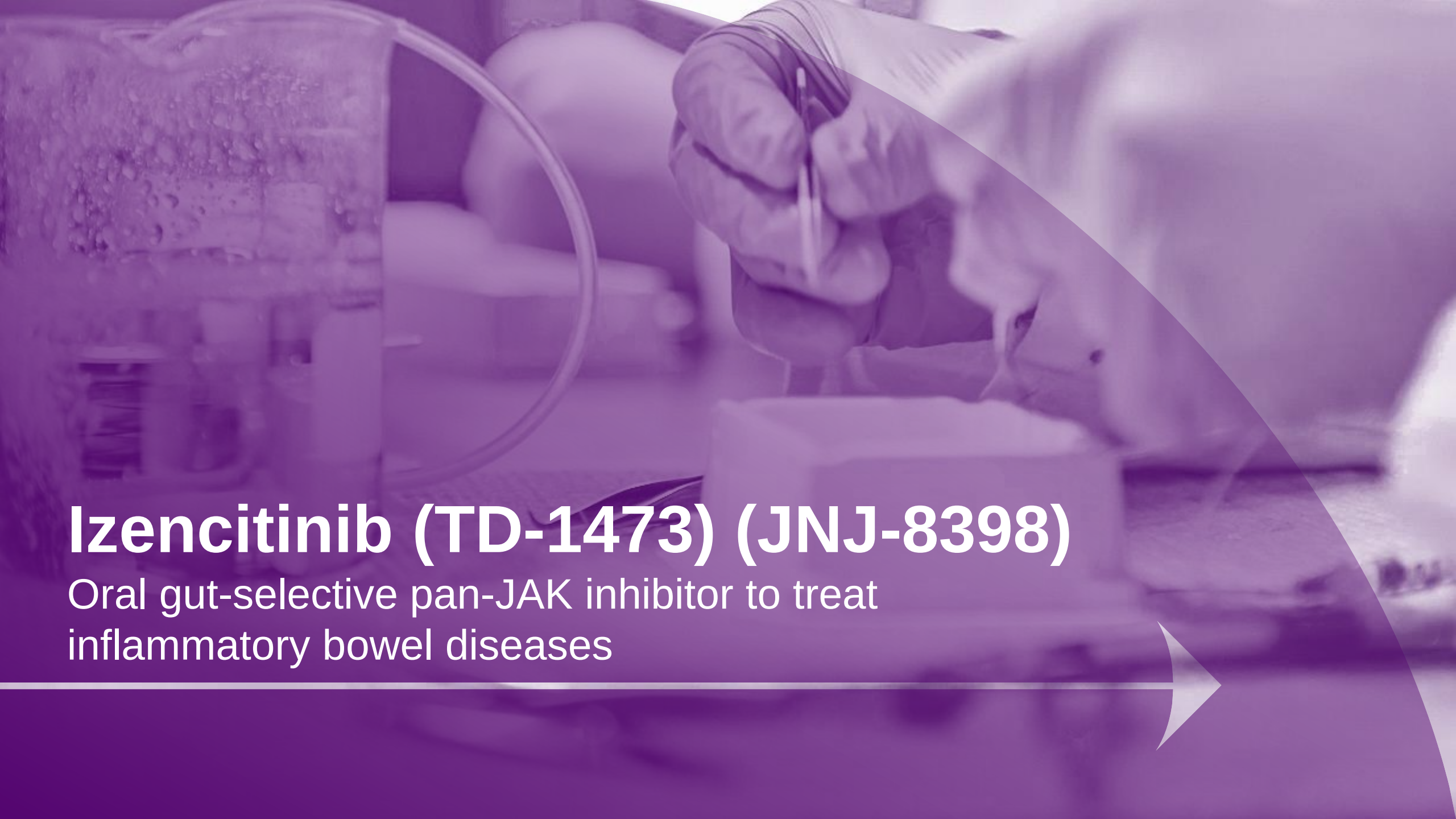
Understanding of current access barriers

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 Parkinson’s and MSA advocacy groups that patients need new therapies to better manage nOH

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

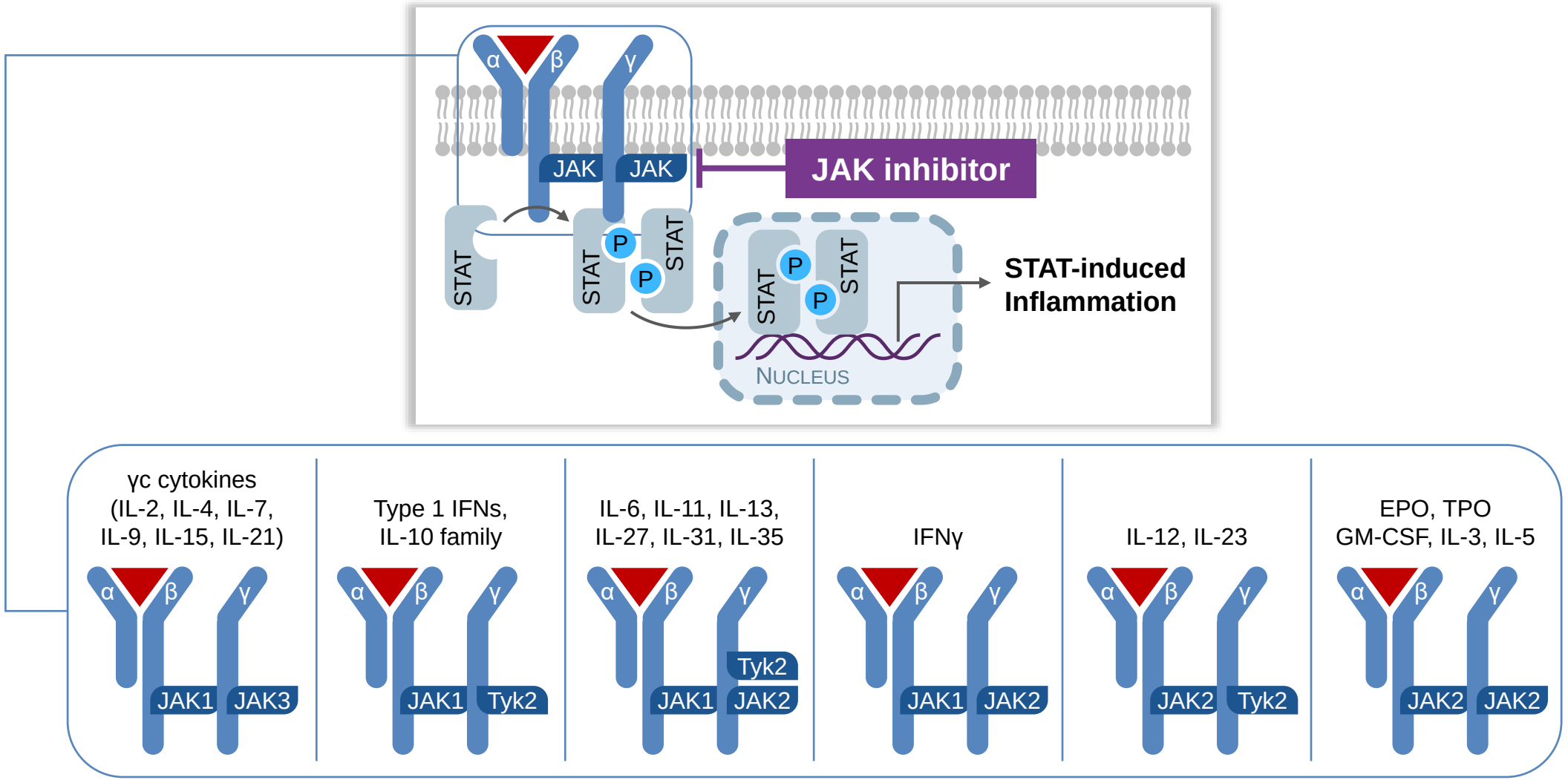
Izencitinib

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
HRQoL, health-related quality of life; IBD, inflammatory bowel disease.

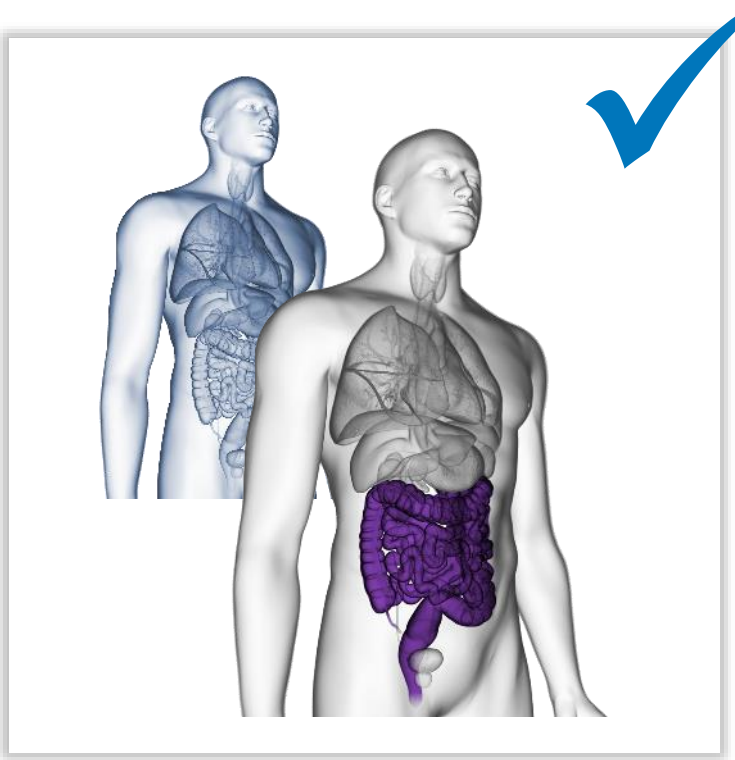
JAK-STAT pathway: orchestrating signaling of multiple pro-inflammatory cytokines



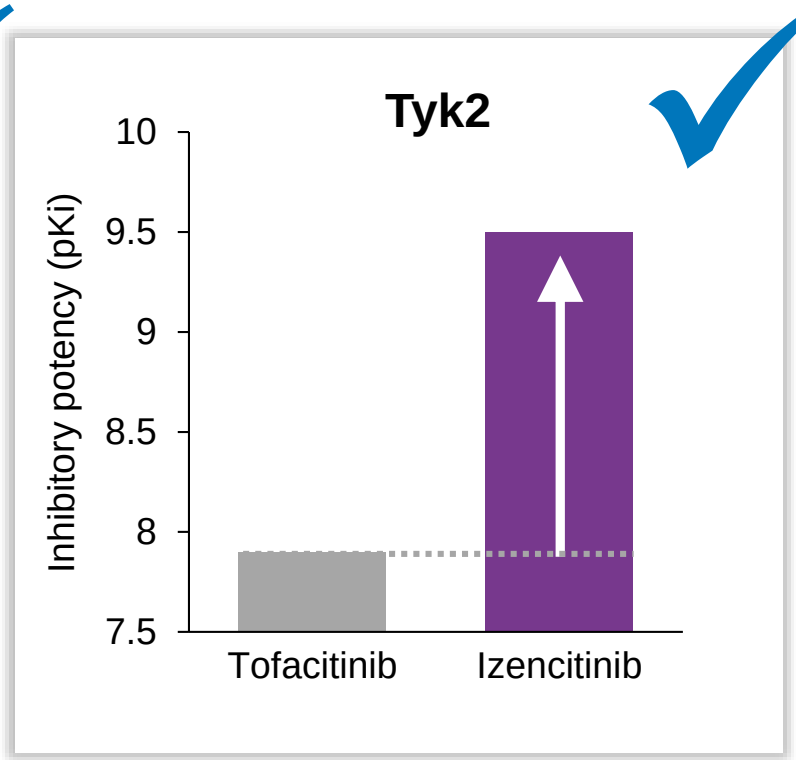
Clark JD, et al. J Med Chem 2014; 57:5023-5038.
EPO, erythropoietin; GM-CSF, granulocyte-macrophage colony-stimulating factor; TPO, thrombopoietin; Tyk, tyrosine kinase.

Izencitinib is an oral, gut-selective pan-JAK inhibitor

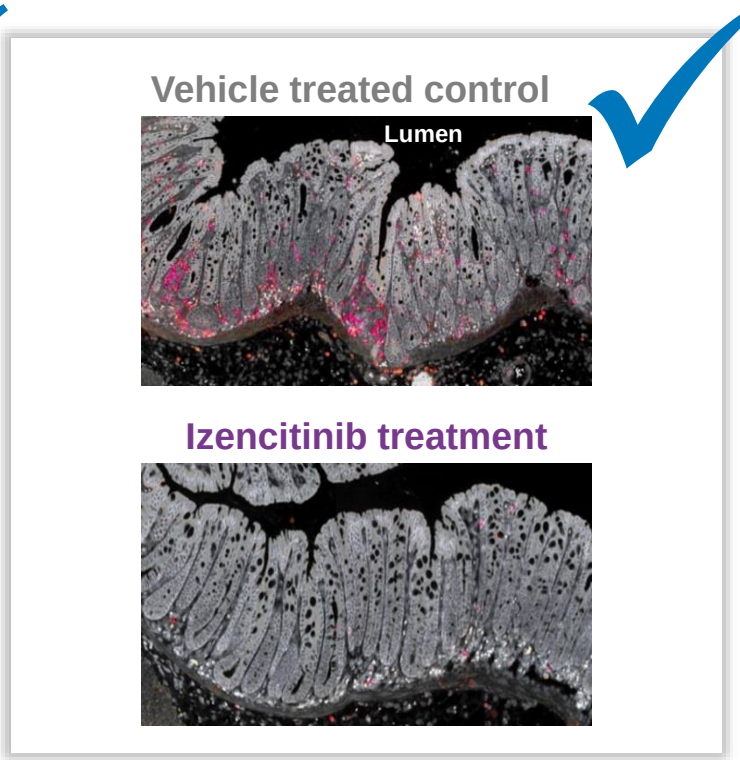
Preclinical data package for Izencitinib represents a potential breakthrough approach to the treatment of IBD



Gut selectivity



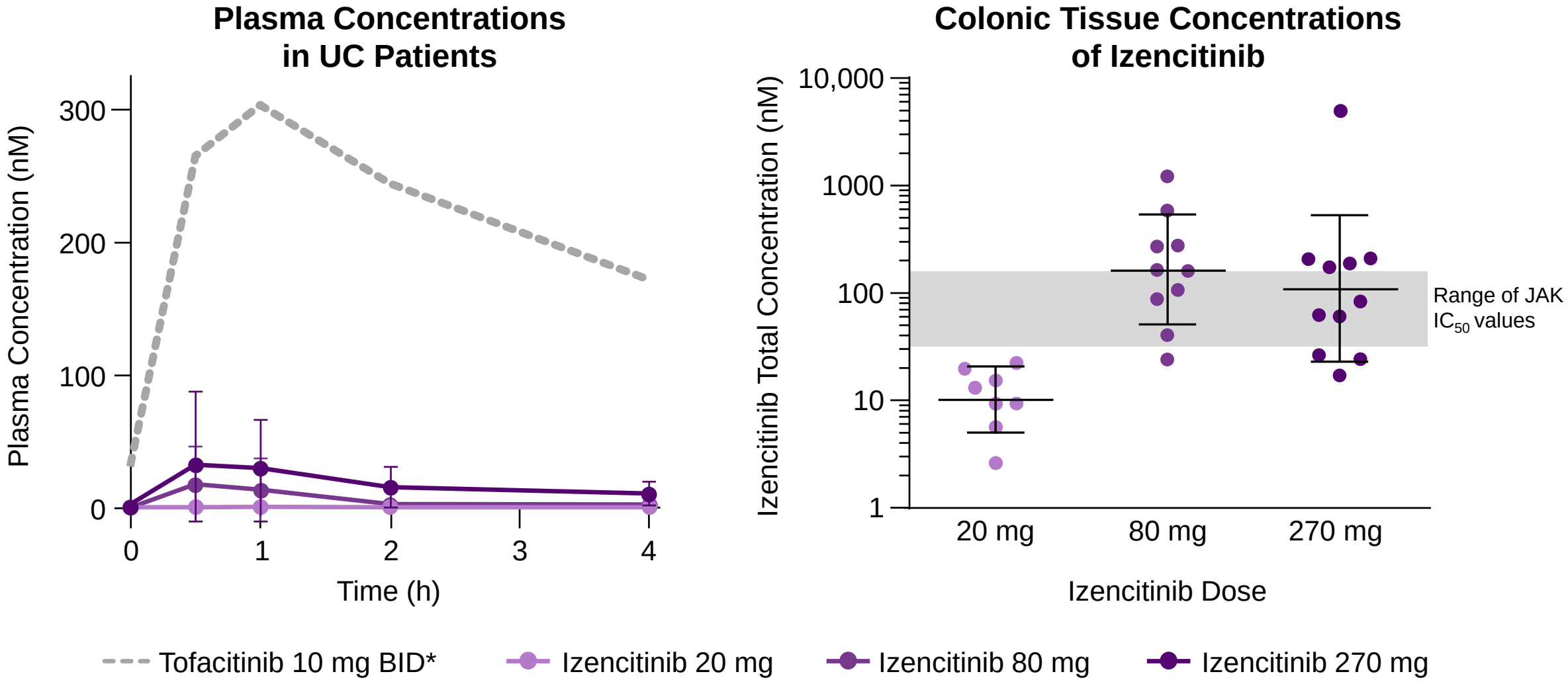
Potent inhibition of Tyk2



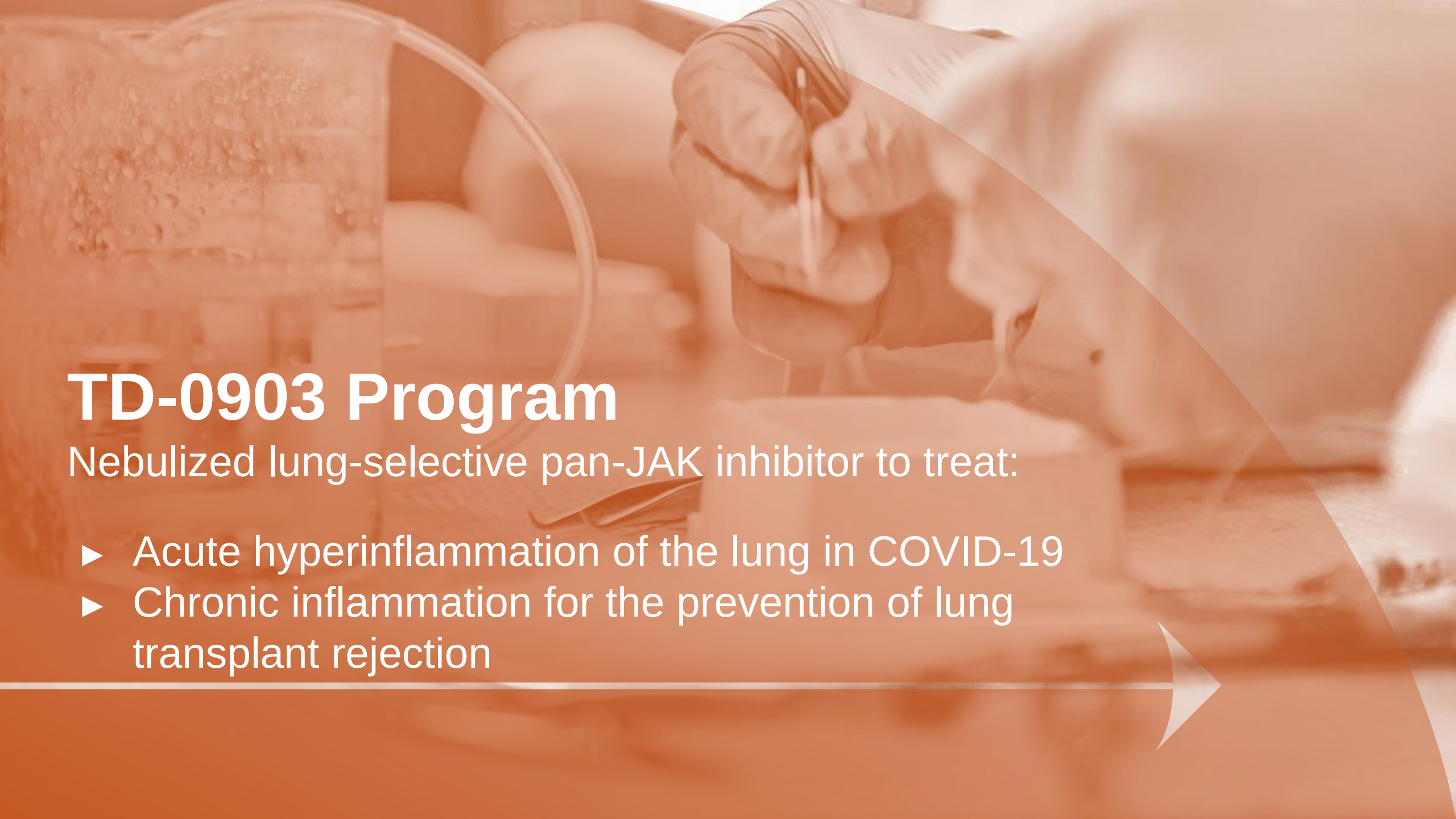
Anti-inflammatory activity in disease model

Journal of Crohn's & Colitis April 20, 2020.

Systemic exposures low; tissue concentrations at or above JAK inhibition levels



*Tofacitinib concentrations extracted from J Pharmacol Exp Ther 348:165–173, January 2014.
BID, twice daily; IC_{50}, concentration to produce 50% maximal inhibition; PK, pharmacokinetics.

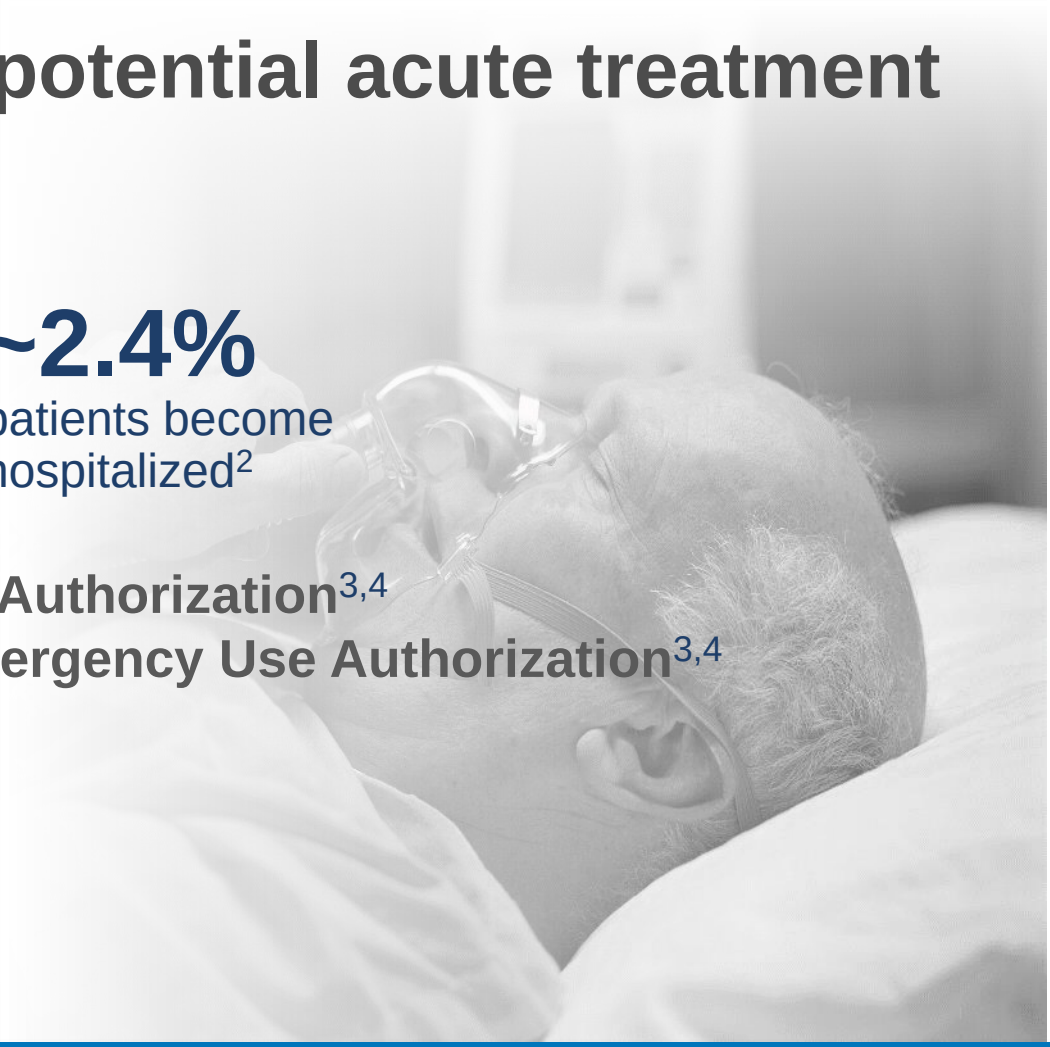


TD-0903 Program

Nebulized lung-selective pan-JAK inhibitor to treat:

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

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



PATIENT POPULATION

>88M patients worldwide[1]

>22M US patients[1] ⋯▸ **~2.4%** patients become hospitalized[2]

CURRENT US TREATMENT LANDSCAPE

2 vaccines available via Emergency Use Authorization[3,4]
1 approved treatment; 8 available via Emergency Use Authorization[3,4]

370 active trials in US[5]

4,266 studies registered worldwide[6]

STRATEGIC OPPORTUNITY

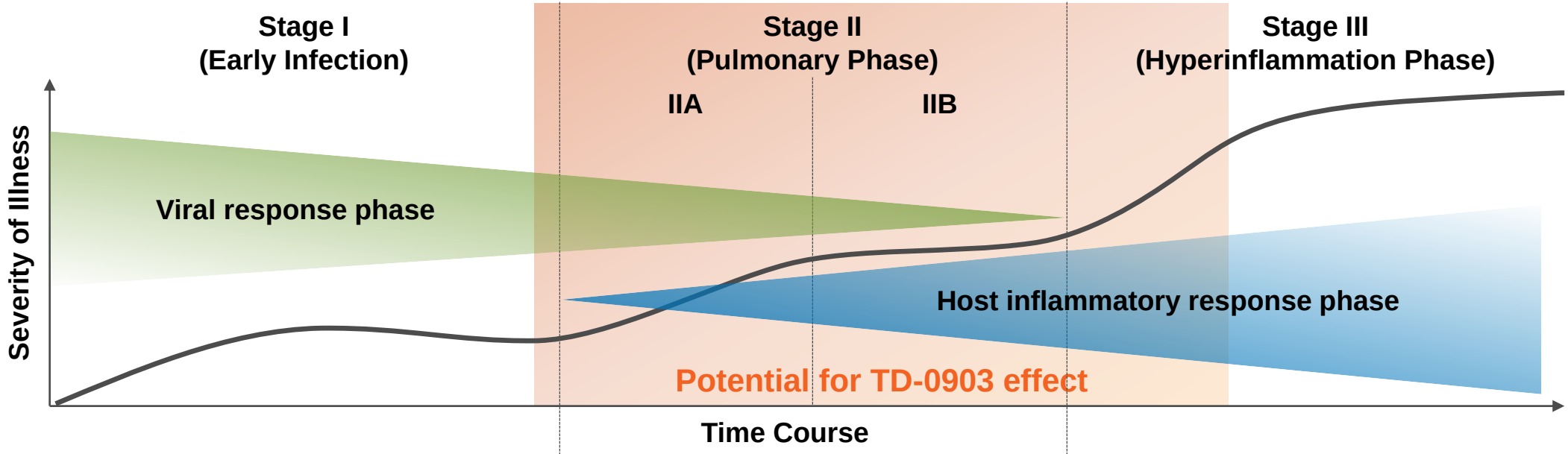
TD-0903

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

Theravance Biopharma
Medicines That Make a Difference

1. https://coronavirus.jhu.edu/map.html, number as of 12/22. 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
5. https://www.fda.gov/media/136832/download#:~:text=This%20EUA%20authorizes%20the%20use,and%20who%20are%20at%20high. 6. https://www.statista.com/statistics/1106306/coronavirus-clinical-trials-worldwide/ According to ClinicalTrials.gov, there are 4,266 studies currently registered which are investigating the coronavirus disease (COVID-19). This statistic shows the total number of results from a search of "covid-19" on ClinicalTrials.gov database, as of December 22, 2020, by region.

Host inflammatory response to COVID-19 drives ALI and ARDS



Clinical symptoms	Mild constitutional symptoms Fever >99.6°F Dry cough, diarrhea, headache	Shortness of breath Hypoxia (PaO_2/FiO_2 ≤300 mmHg)	ARDS SIRS/shock Cardiac failure
Clinical signs	Lymphopenia, increased prothrombin time, increased D-Dimer and LDH (mild)	Abnormal chest imaging Transaminitis Low normal procalcitonin	Elevated inflammatory markers (CRP, LDH, IL-6, D-dimer, ferritin) Troponin, NT-proBNP elevation

Theravance Biopharma
Medicines That Make a Difference

ALI Acute Lung Injury; ARDS, Acute respiratory distress syndrome
Adapted from Siddiqi HK, et al. J Heart Lung Transplant 2020 Mar 20.
CRP, C-reactive protein; LDH, lactate dehydrogenase; NT-proBNP, ventricular natriuretic peptide; SIRS, severe inflammatory response syndrome.

TD-0903: Development plan designed to progress rapidly

Phase 1: Healthy volunteers

Single ascending dose: → **Multiple ascending dose x 7 days:**

Single-dose safety, tolerability, PK → Repeat-dose safety, tolerability, PK

Complete

Phase 2: Hospitalized COVID-19 patients

Part 1 — Multiple-ascending dose study x 7 days: Repeat-dose safety, tolerability, PK, early dose-dependent efficacy

Complete

Part 2 — Parallel group study x 7 days: Proof of concept efficacy and safety

- Dose 3 mg + SOC
- Placebo + SOC

Ongoing

SOC, standard of care.

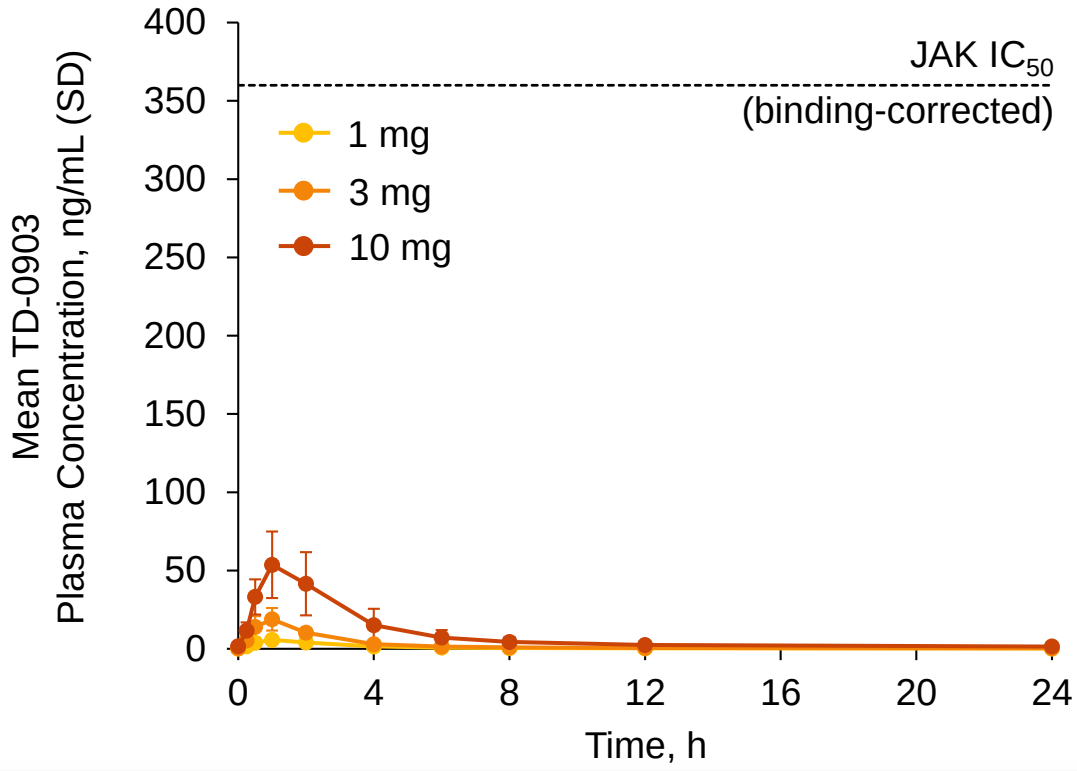
TD-0903 Phase 1 supports initiation of Phase 2 in COVID-19

Nebulized lung-selective pan-JAK inhibitor to treat acute hyperinflammation of the lung in COVID-19

Safety and Tolerability

- TD-0903 was well tolerated as single daily doses across a dose range from 1 mg to 10 mg for 7 days in healthy subjects
- Adverse events were assessed to be mild or moderate in severity, and none led to discontinuation of study treatment
- No clinically relevant changes in laboratory parameters, vital signs, or ECGs

Systemic Pharmacokinetics



Favorable safety and tolerability profile and PK below levels anticipated to exert systemic effects

IC_{50}, half-maximal inhibitory concentration; SD, standard deviation.

First-in-disease opportunity for the prevention of lung transplant rejection

PATIENT POPULATION

Lung transplants have the poorest prognosis of all solid organ transplants
COPD, IPF, and CF top 3 diagnoses driving need for lung transplantation

6,240
lung transplants worldwide, 2019[1]

2,714
lung transplants per year in US[2]

15%
CAGR since 1988[2]

~50%
mortality at 6 years post transplant[3]

$3.5B
medical/productivity costs (2015–2025)[4]

CURRENT TREATMENT LANDSCAPE

No FDA-approved therapies to prevent lung transplant rejection or CLAD

Current standard of care: triple immunosuppression therapy

- Calcineurin inhibitors (tacrolimus)
- Anti-proliferative agents (MMF)
- Corticosteroids
- IL-2 mAb induction therapy (basiliximab)

STRATEGIC OPPORTUNITY

TD-0903

Potential first approved therapy specifically to prevent acute lung transplant rejection and development of CLAD
Use following lung transplantation could potentially improve patient morbidity and mortality risk, and reduce need for re-transplantation

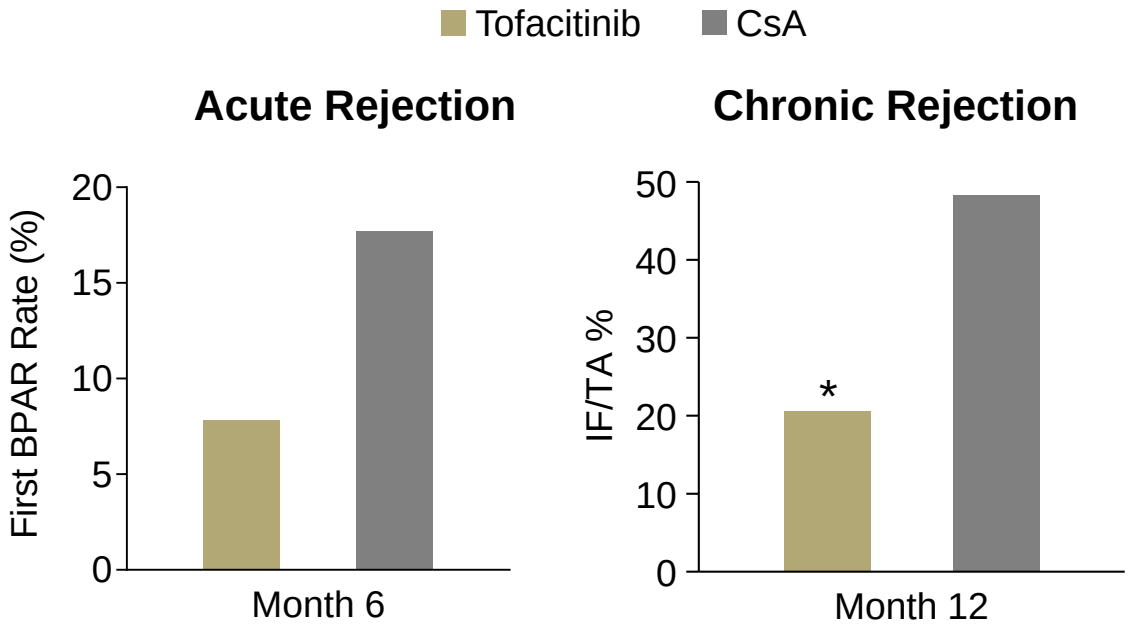
Theravance Biopharma
Medicines That Make a Difference

1. http://www.transplant-observatory.org/data-charts-and-tables/.
2. United Network for Organ Sharing (UNOS), https://unos.org/data/transplant-trends.
3. Chambers DC et al, JHLT 2018; 37(10): 1169-1183. 4. JHEOR. 2015. CA Jones https://pdfs.semanticscholar.org/108c/5cb16aaab19fa9e9a1ccba64ae5869336f26.pdf
CAGR, compound annual growth rate; IPF, idiopathic pulmonary fibrosis; CF, cystic fibrosis; CLAD, chronic lung allograft dysfunction; mAb, monoclonal antibody; MMF, mycophenolate mofetil.

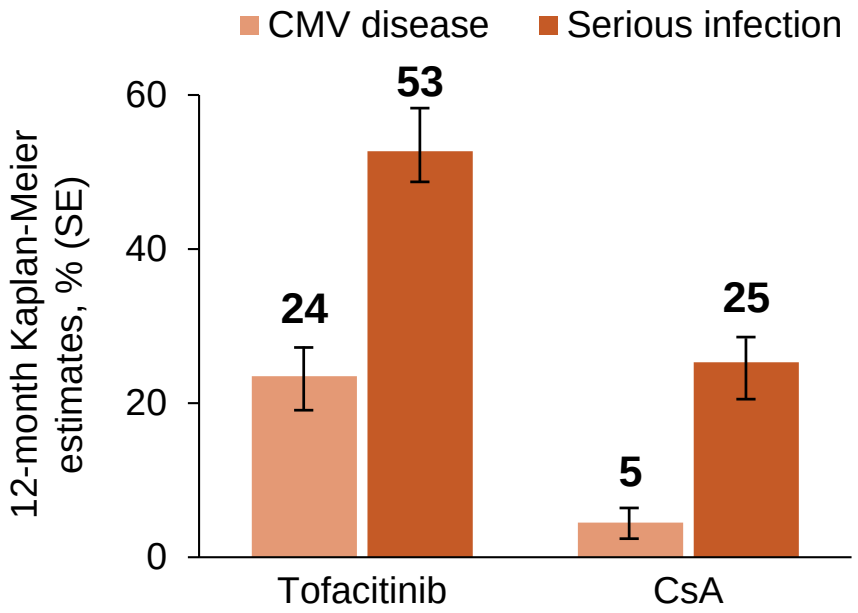
Pan-JAK inhibitors can prevent transplant rejections

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; SE, standard error; TWC2, time-weighted 2-h post-dose concentrations.

TD-8236

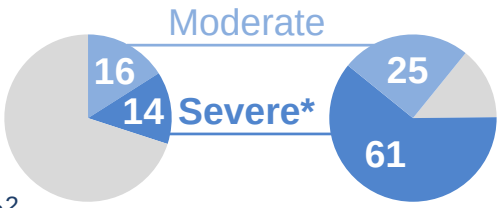
Potential first inhaled JAKi for asthma

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

Theravance Biopharma
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., The economic burden of asthma in the United States, 2008-2013. Ann Am Thorac Soc. 2018; 15(3):348-356 5. TBPH estimate based on multiple data sources.
ICS, inhaled corticosteroids; IFN, interferon; LABA, long-acting β2 agonists; LTRA, leukotriene receptor antagonist; OCS, oral corticosteroid; T2, type 2; TSLP, thymic stromal lymphopoietin.

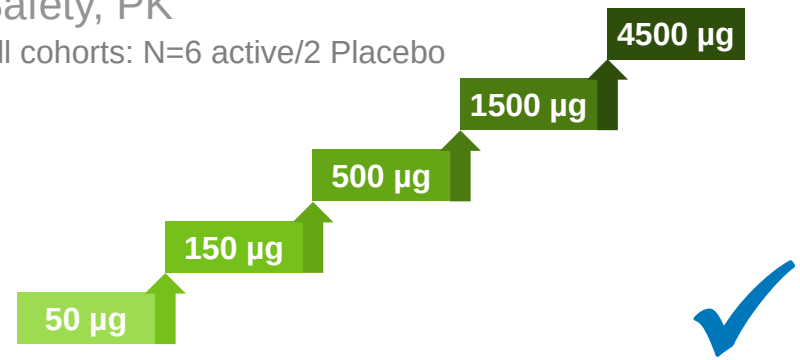
TD-8236: Phase 1 clinical trial design

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

Part A: SAD (Healthy volunteers)

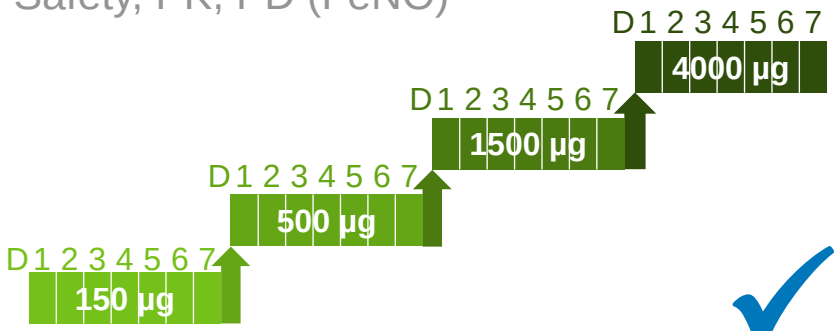
Safety, PK

All cohorts: N=6 active/2 Placebo



Part B: MAD (Mild asthmatics)

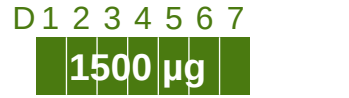
Safety, PK, PD (FeNO)

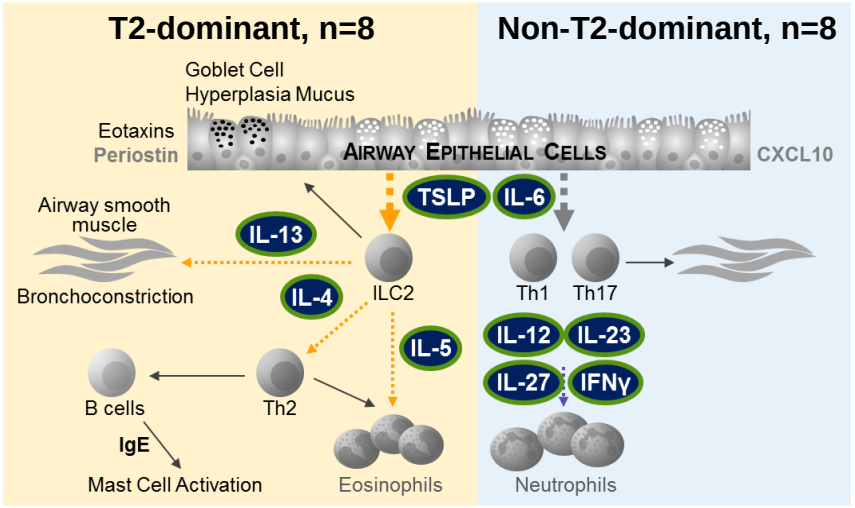


Part C: MoA Biomarkers

(Moderate-to-severe asthmatics + ICS)

N=16 active/8 placebo





- 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

FeNO, fractional exhaled nitric oxide; ICS, inhaled corticosteroids; MAD, multiple-ascending dose; MoA, Mechanism of Action; PK, pharmacokinetic; PD, pharmacodynamic; pSTAT, phosphorylated signal transducer and activator of transcription; SAD, single-ascending dose.

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

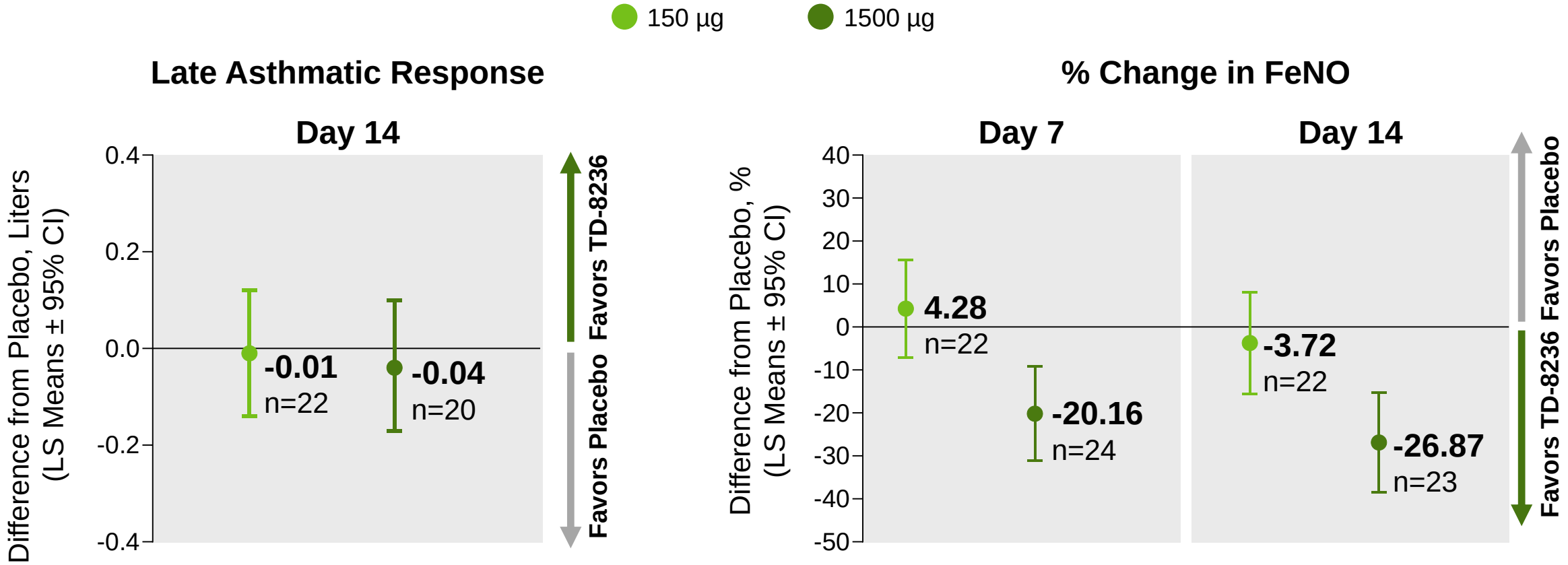
Phase 1 Profile	Healthy Volunteer Single Dose (Part A)	Mild Asthma Multiple Dose (Part B)	Moderate-to-Severe Asthma [+ ICS] Multiple Dose (Part C)
Generally well tolerated	✓	✓	✓
Minimal systemic exposure	✓	✓	✓
PK and PD profile consistent with once-daily dosing	✓	✓	✓
Biologic activity in lungs of patients 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 inhaled corticosteroids
- Ongoing analysis of effect of TD-8236 on additional biomarkers including cytokines and gene expression

ICS, inhaled corticosteroids; PK, pharmacokinetic; PD, pharmacodynamic; FeNO, fractional exhaled nitric oxide

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

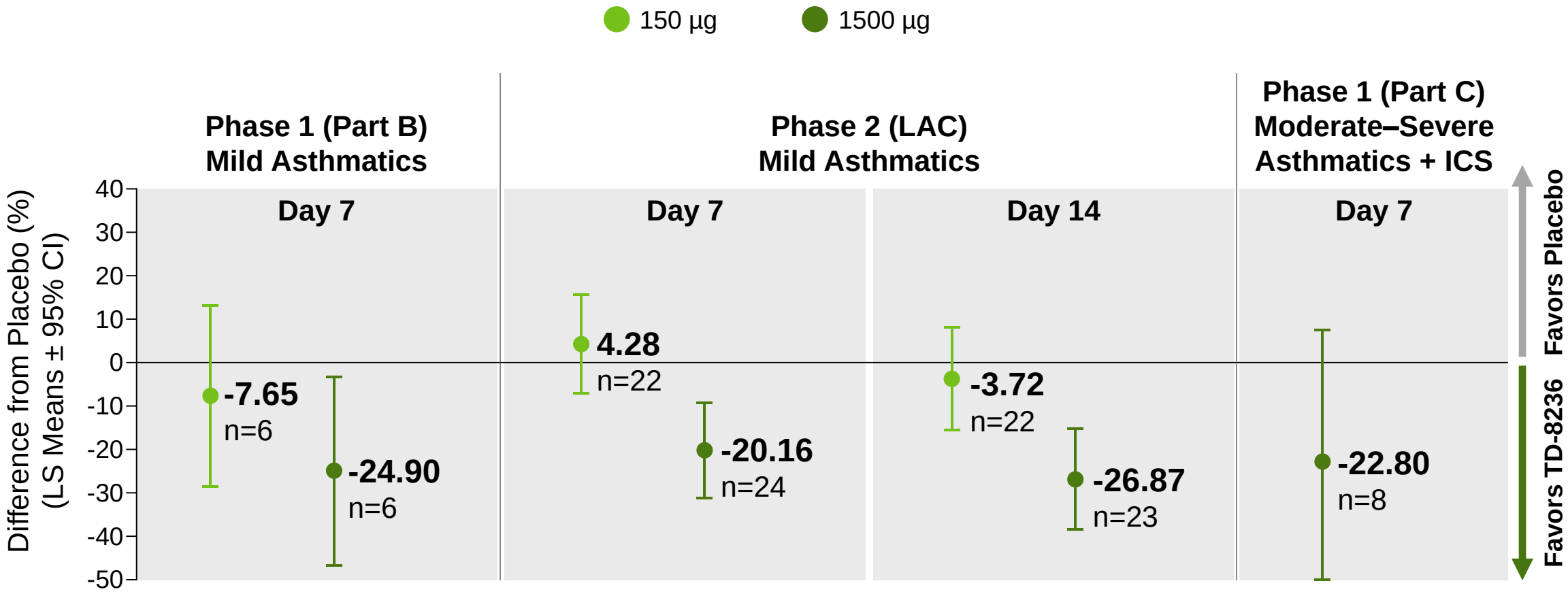
Significant reductions in inflammation marker (FeNO) and favorable safety and tolerability



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

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

TD-8236 FeNO reductions consistent across Phase 1 and 2



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

ICS, inhaled corticosteroids; LAC, lung allergen challenge; LS, least-squares; CI, confidence interval.

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]

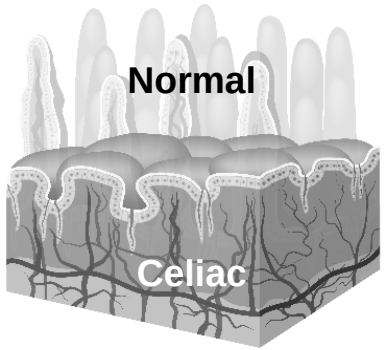
4–4.5x
increase in US over past 50 y[4]

>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

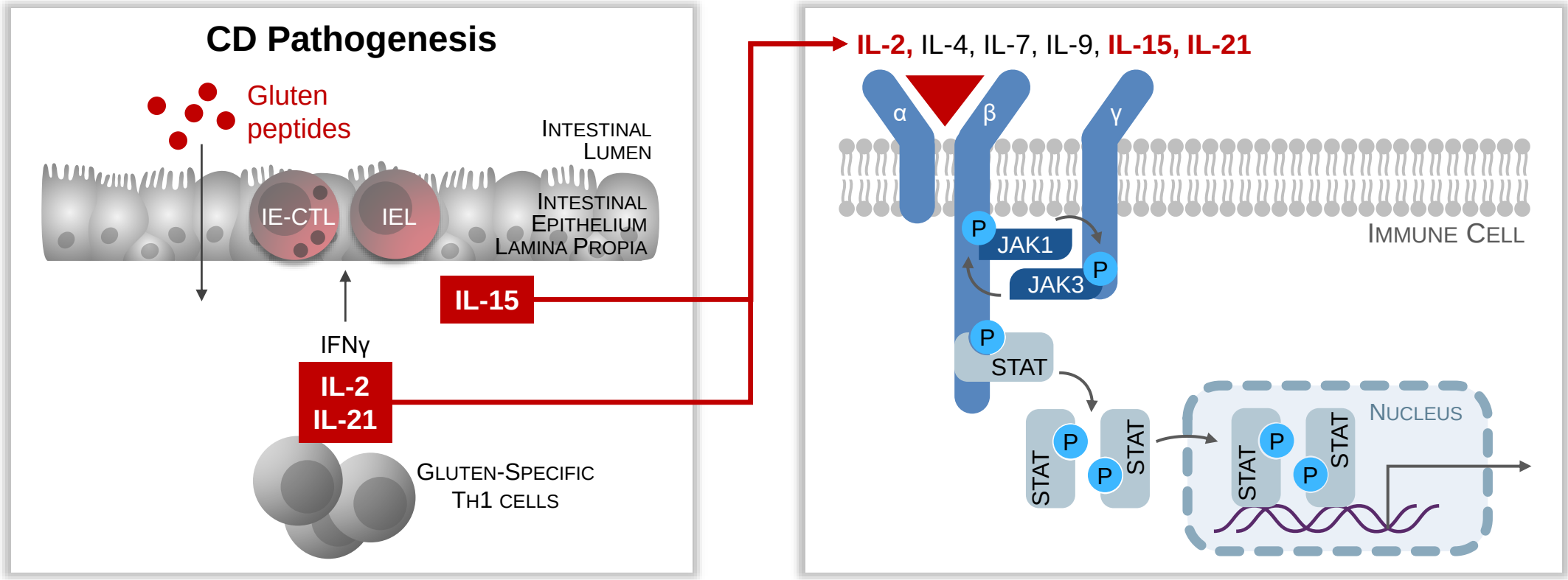
TD-5202

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

Theravance Biopharma
Medicines That Make a Difference

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. Dermatitis Herpetiformis: A Common Extraintestinal Manifestation of Coeliac Disease. Nutrients 2018;10(5). pii: E602
5. Guandalini et al. Direct Costs in Patients with Celiac Disease in the USA: A Retrospective Claims Analysis. Digestive Diseases Sciences 2016; 61(10):2823-30 6. Theravance Market Research.

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

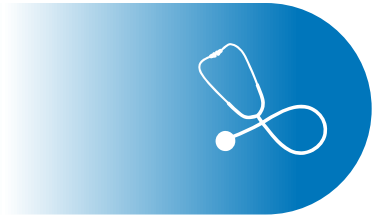


- Proof-of-relevance from recent positive Phase 2 data with systemic JAK3 inhibitor in alopecia areata, another T-cell mediated disease
- Localized JAK3 inhibition has the potential to avoid systemic immunosuppression (genetic JAK3 deficiency leads to severe immunodeficiency)

Figure adapted from Jabri B and Sollid L. J Immunol 2017;198:3005-14.
IE-CTL, intraepithelial cytotoxic lymphocyte; IEL, intraepithelial lymphocyte.

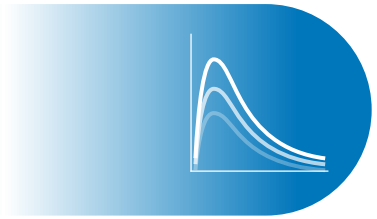
TD-5202 First-in-human overall results summary

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; $C_{max,ss}$, maximal steady-state concentration; 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

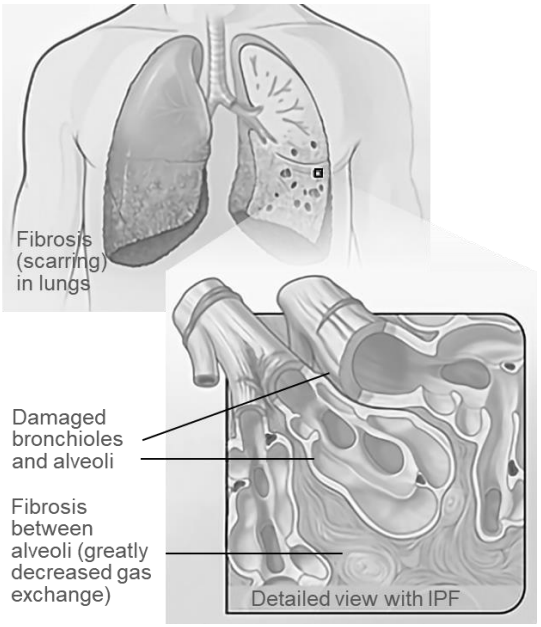
PATIENT POPULATION

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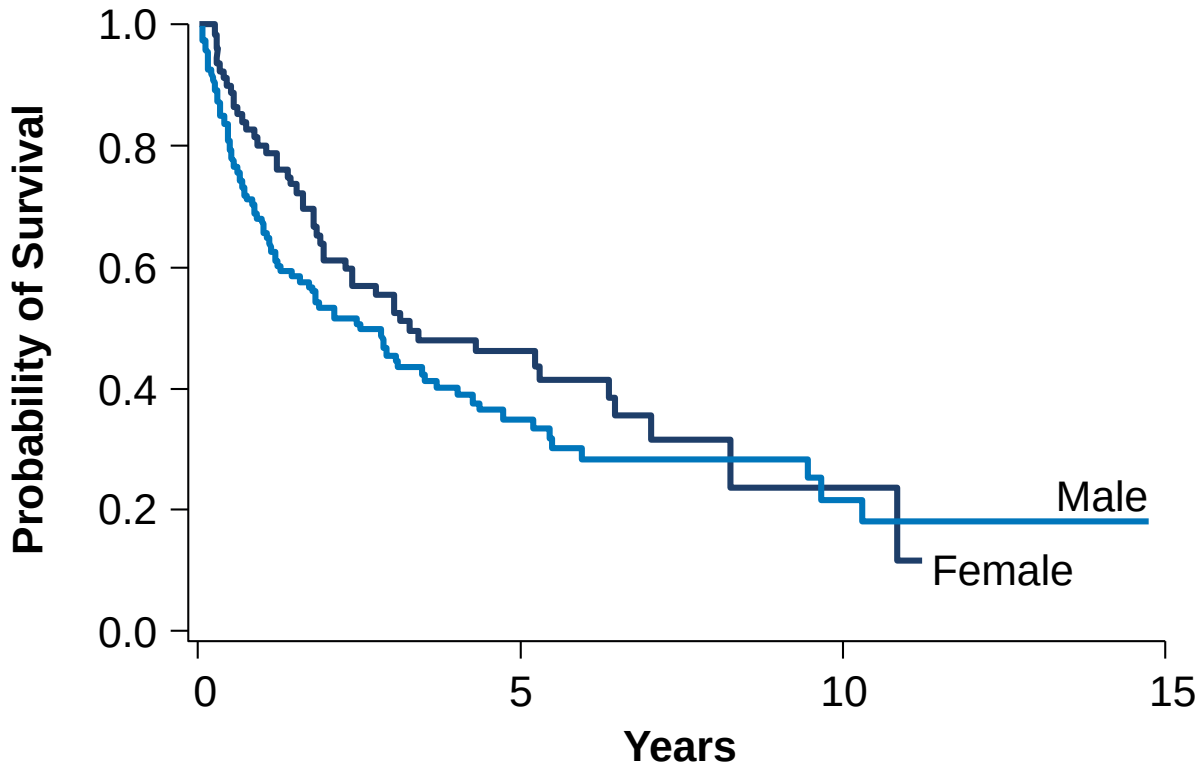
1. Raghu G, et al. Lancet Resp. 2014: 2(7):566-572.
2. Raghu G, et al. Eur Respir J. 2016: 48(1):179-186.
3. National Heart Lung and Blood Institute (NIH), Public Domain, https://commons.wikimedia.org/w/index.php?curid=29590103. Soc, Standard of Care.

Significant opportunity remains for effective IPF treatments



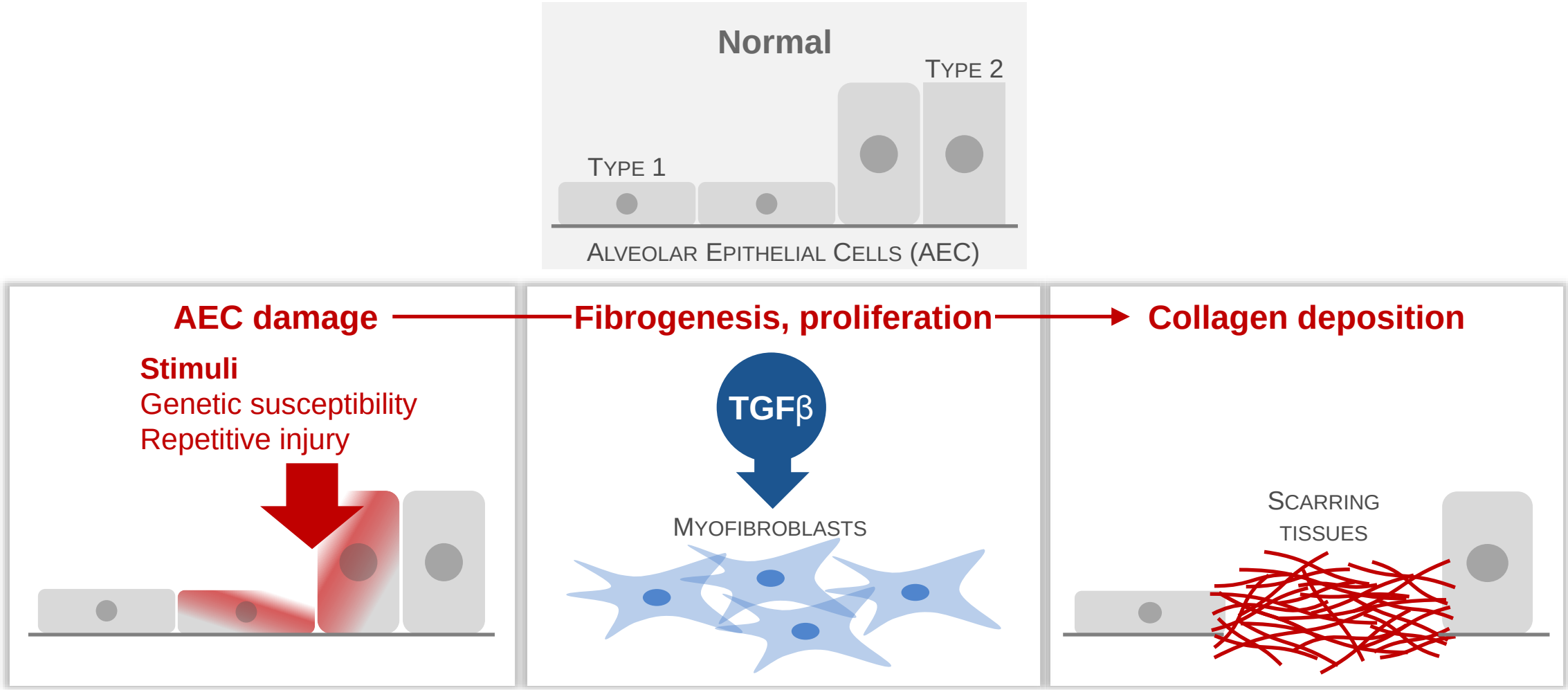
- Mortality with IPF remains high
  - <50% alive 3 years after diagnosis[1]

Goal To arrest disease progression with improved tolerability

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

Targeting the TGFβ pathway

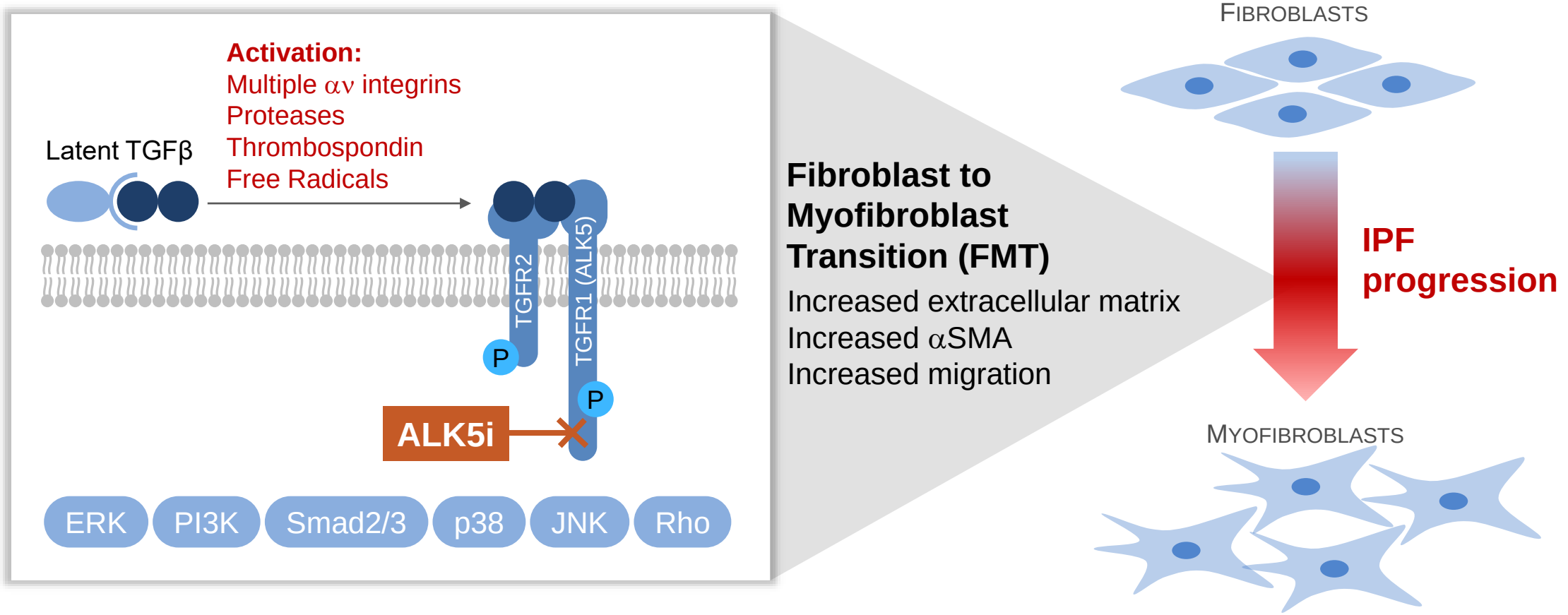
A core signaling pathway that drives fibrosis



TGFβ, transforming growth factor β.

Selectively targeting the TGFβ pathway through ALK5 inhibition

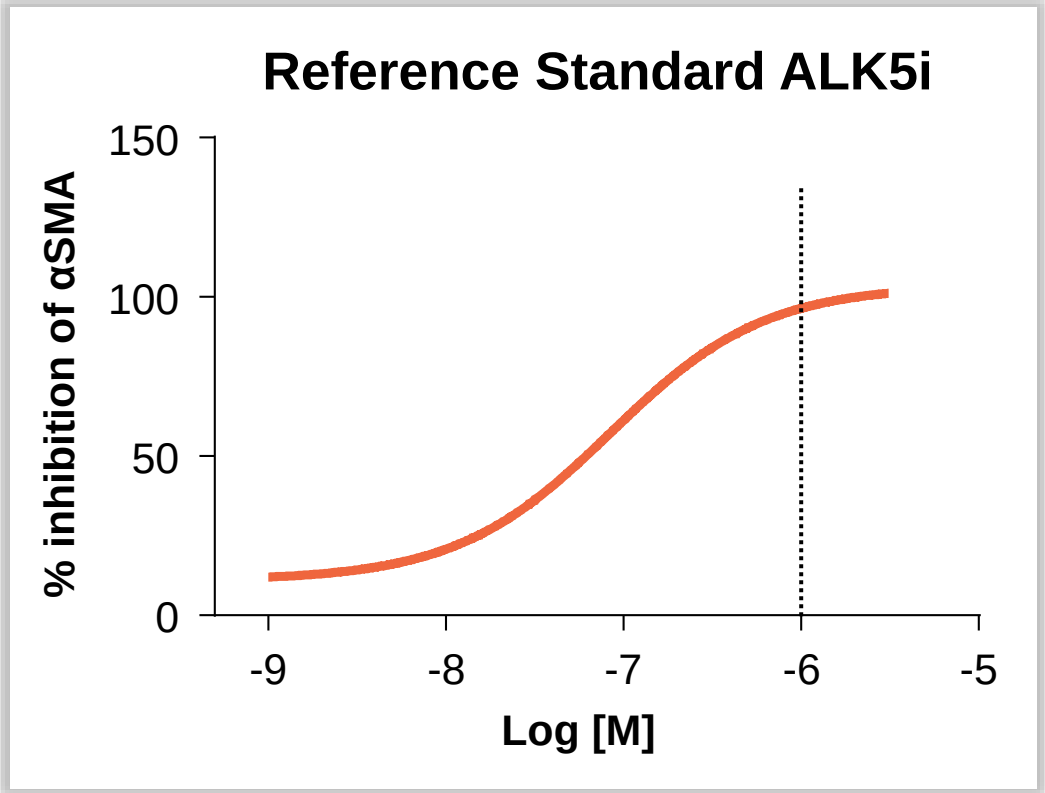
Inhibiting a core signaling pathway that drives fibrosis regardless of activation mechanism

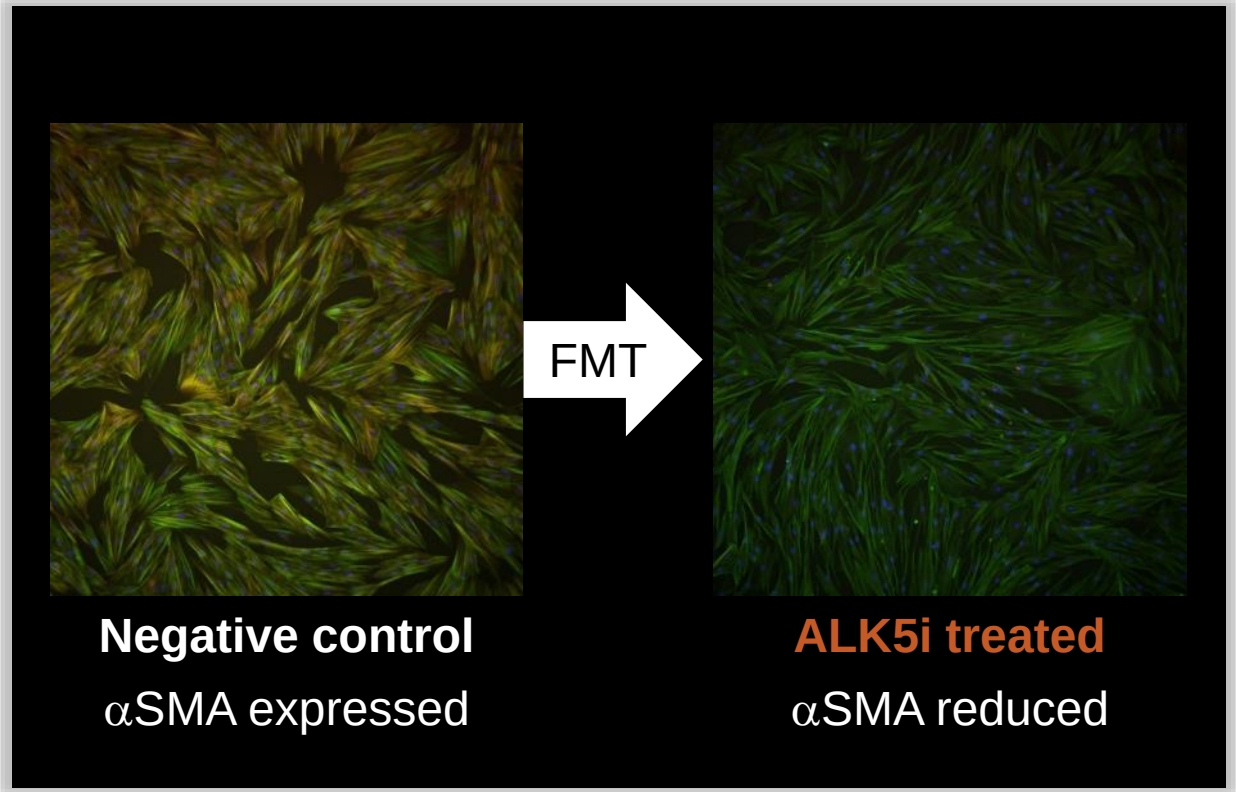


αSMA , α-smooth muscle actin; ERK, extracellular signal-regulated kinase; JNK, c-Jun N-terminal kinase; PI3K, phosphatidylinositol-4,5-bisphosphate 3-kinase; Smad2/3, mothers against decapentaplegic homolog 2/3; TGFR (ALK5), TGFβ receptor.

Adapted from: Neuzillet C, et al. Oncotarget 2013;5:78–94.

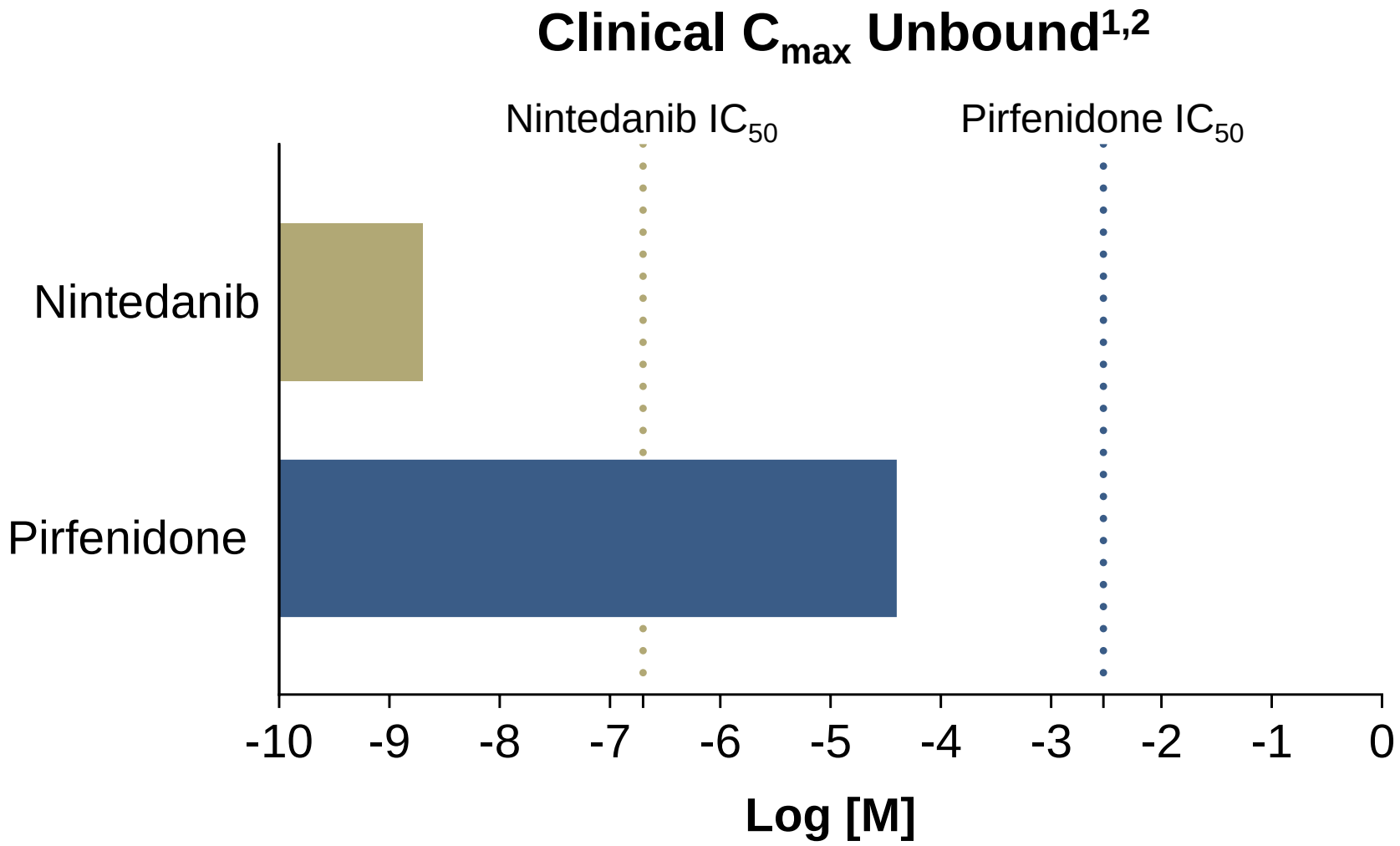
ALK5 inhibition directly interrupts FMT[1] in IPF





FTM, fibroblast to myofibroblast transition

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

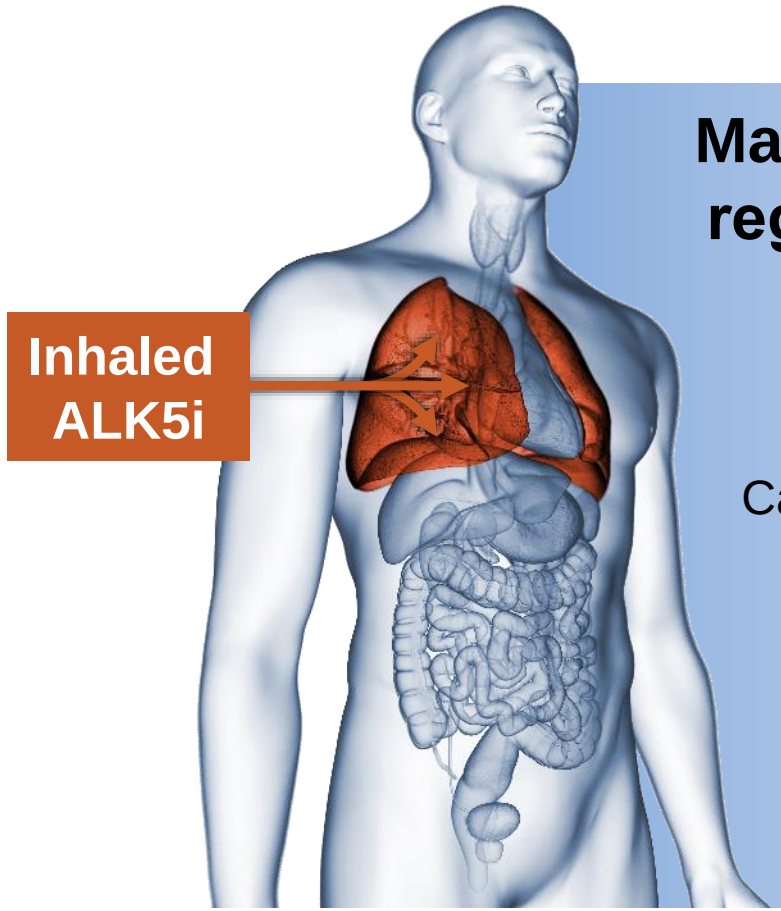


FTM, fibroblast to myofibroblast transition; C_{max}, maximal concentration; IC_{50}, half maximal inhibitory concentration.

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.

Lung selectivity avoids unwanted systemic side effects

Minimizing systemic inhibition of a cytokine essential for homeostasis



Maintaining key systemic regulatory roles of TGFβ

Wound repair
Bone healing
Cardiovascular homeostasis
Tumor suppression
Endocrine function

Modified from: Akhurst RJ, Hata A. Nat Rev Drug Discov 2012;11:790-811.
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

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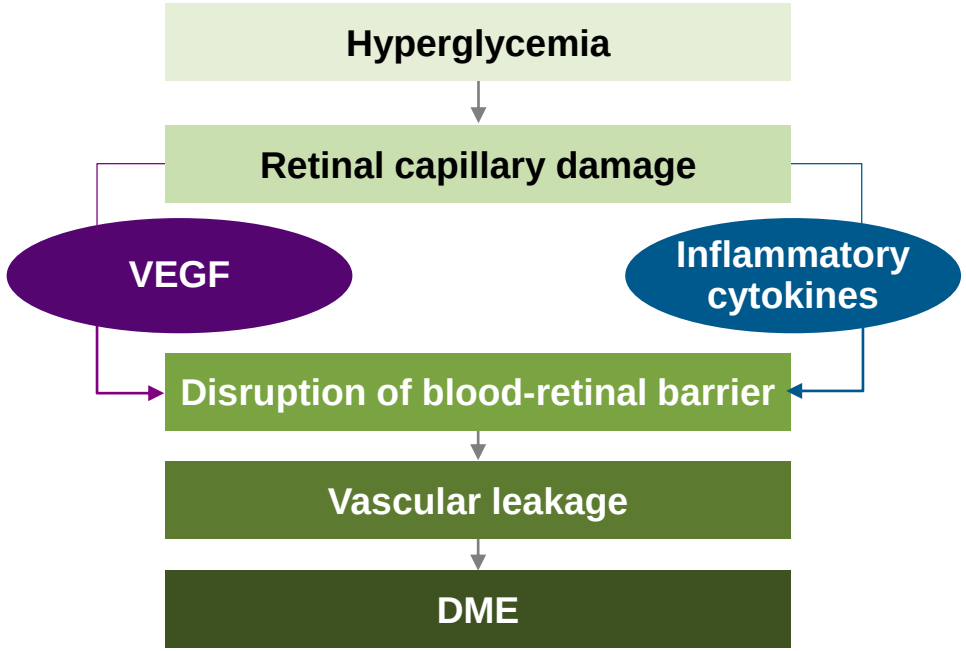
2. Romero-Aroca, World J Diabetes 2011;2(6): 98-104. 3. Lee et al Curr Med Res Opin 2008;24:1549-59.
Images from Angiogenesis Foundation, www.scienceofdme.org. DME, Diabetic macular edema; VEGFi, vascular endothelial growth factor inhibitor.

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

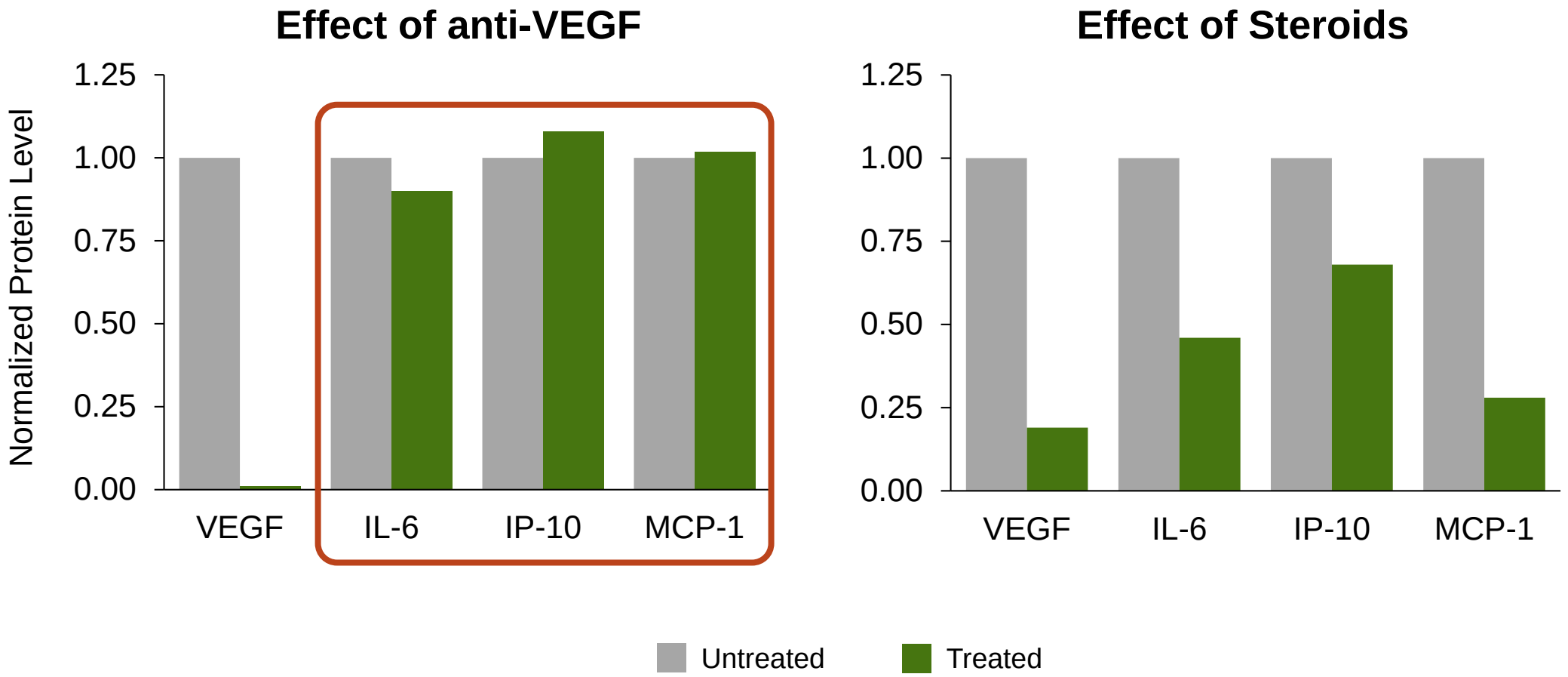
Intraocular steroids

- High frequency of formation of cataracts and glaucoma

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

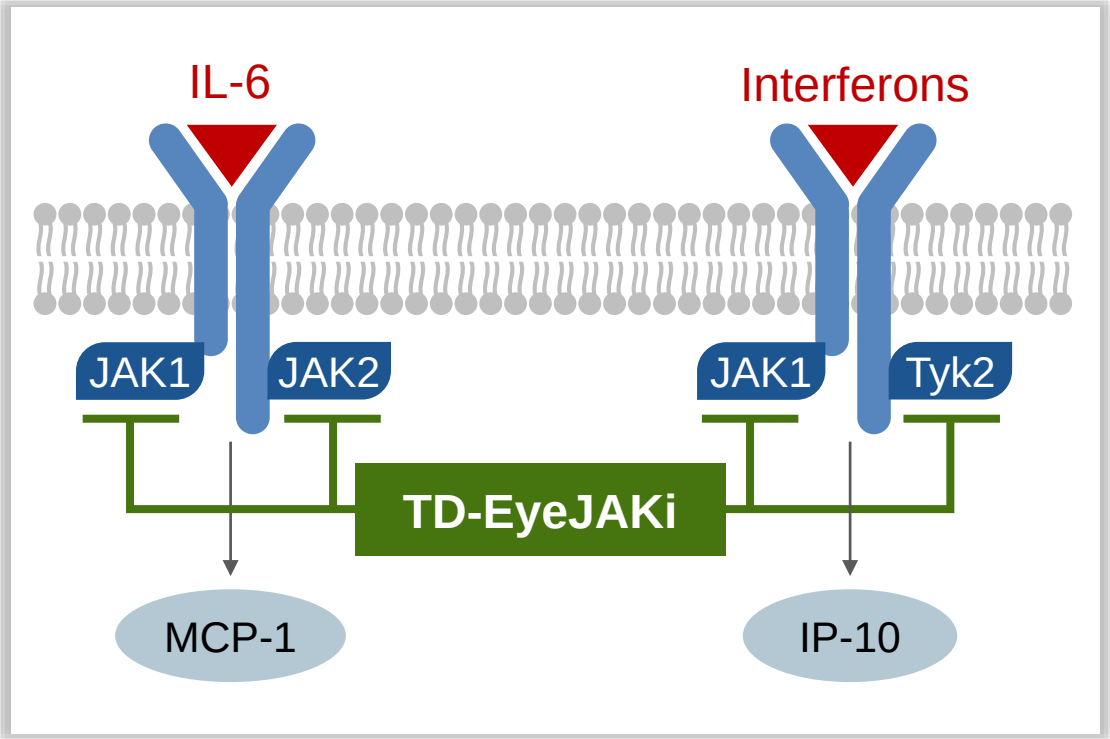
Gonzalez VH, et al. Am J Ophthalmol 2016;172:72-79.
VEGF, vascular endothelial growth factor.

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



Adapted from Sohn HJ, et. al. Am J Ophthalmol 2011; 152:686-694.

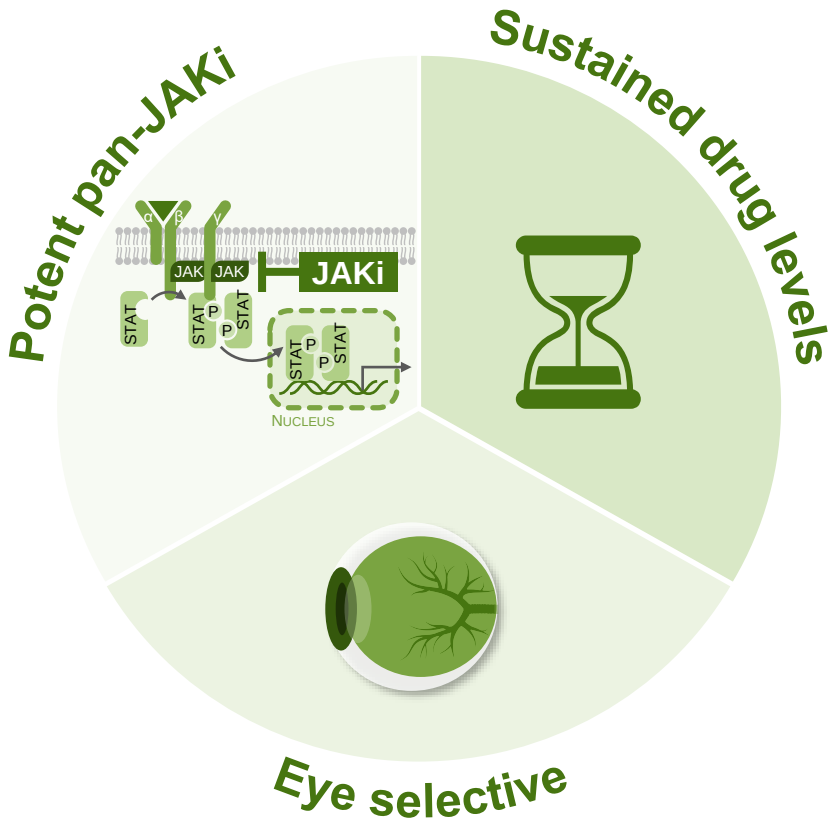
Ocular pan-JAK inhibition has the potential to address key disease pathways in DME

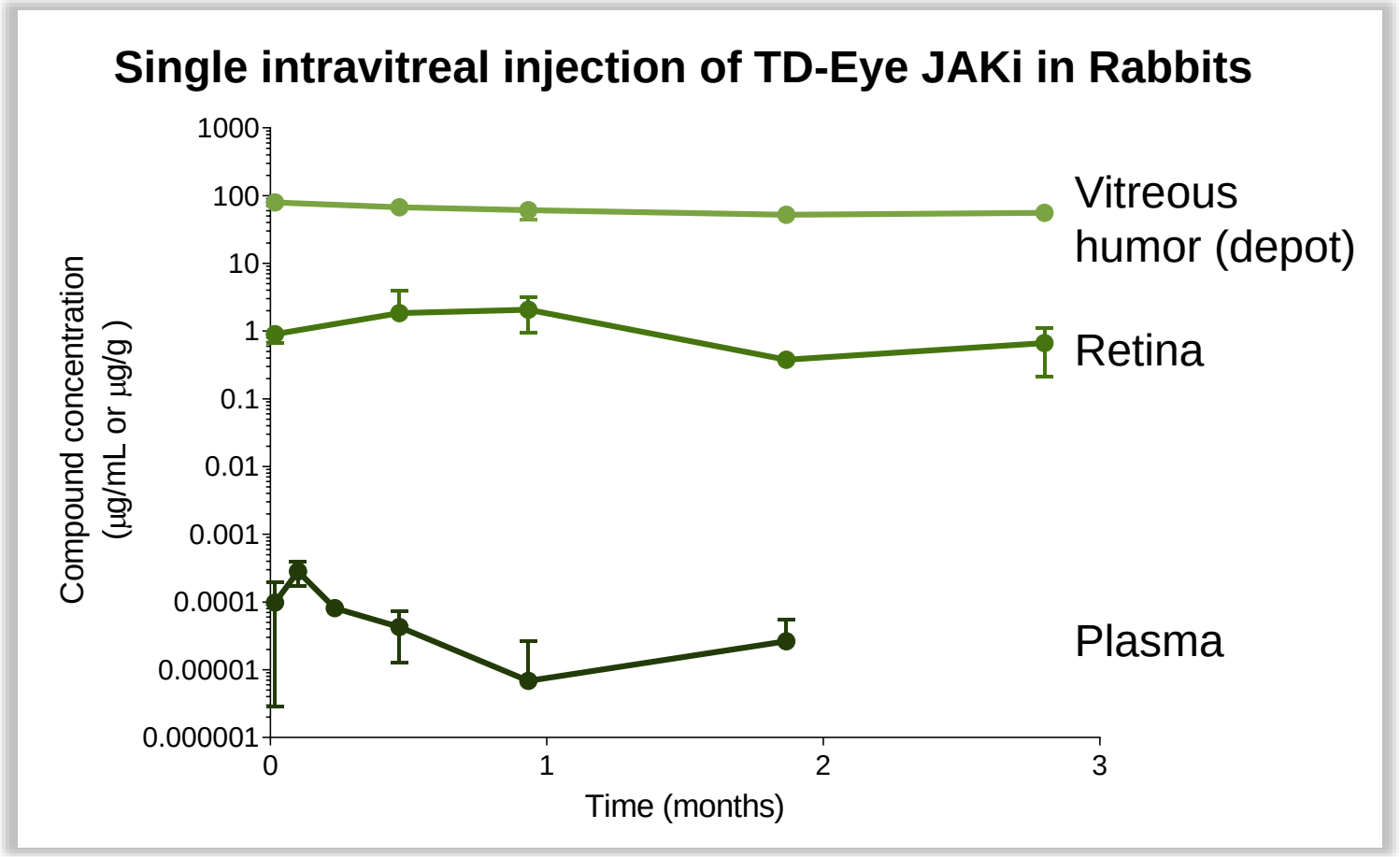


TD-EyeJAKi inhibits key DME inflammatory pathways:

- 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*

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





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.

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.