Investor Presentation

August 2026

We're in.
For patients.

Forward Looking Statements

The forward-looking statements in this presentation are based upon the Company's current expectations and beliefs, and involve known and unknown risks, uncertainties and other factors, which may cause the Company's actual results, performance and achievements and the timing of certain events to differ materially from the results, performance, achievements or timings discussed, projected, anticipated or indicated in any forward-looking statements. Such risks, uncertainties and other factors include, among others, the following: failure to continue to successfully commercialize ARIKAYCE® in the U.S., Europe or Japan or failure to successfully commercialize BRINSUPRI® in the U.S. or Europe, or to maintain U.S., European or Japanese approval for ARIKAYCE or U.S. or E.U. approval for BRINSUPRI; our inability to obtain full approval of ARIKAYCE from the FDA, including the risk that we will not successfully or in a timely manner complete the confirmatory post-marketing clinical trial required for full approval of ARIKAYCE, or our failure to obtain regulatory approval to expand ARIKAYCE's indication to a broader patient population; failure to obtain, or delays in obtaining, regulatory approvals for our product candidates in the U.S., Europe or Japan, for ARIKAYCE outside of the U.S., Europe and Japan, including separate regulatory approval for the Lamira® Nebulizer System in each market and for each usage, or for BRINSUPRI outside of the U.S. and the E.U.; failure to successfully commercialize our product candidates, if approved by applicable regulatory authorities, or to maintain applicable regulatory approvals for such product candidates, if approved; uncertainties or changes in the degree of market acceptance of our marketed products or, if approved, our product candidates, by physicians, patients, third-party payors and others in the healthcare community; our inability to obtain and maintain adequate reimbursement from government or third-party payors for our marketed products or, if approved, our product candidates, or acceptable prices for our marketed products or, if approved, our product candidates; inaccuracies in our estimates of the size of the potential markets for our marketed products and our product candidates or in data we have used to identify physicians, expected rates of patient uptake, duration of expected treatment, or expected patient adherence or discontinuation rates; failure of third parties on which we are dependent to manufacture sufficient quantities of our marketed products and our product candidates for commercial or clinical needs, as applicable, to conduct our clinical trials, or to comply with our agreements or laws and regulations that impact our business; risks and uncertainties associated with, and the perceived benefits of, our senior secured loan with certain funds managed by Pharmakon Advisors, LP and our royalty financing with OrbiMed Royalty & Credit Opportunities IV, LP, including our ability to maintain compliance with the covenants in the agreements for the senior secured loan and royalty financing and the impact of the restrictions on our operations under these agreements; our inability to create or maintain an effective direct sales and marketing infrastructure or to partner with third parties that offer such an infrastructure for distribution of our marketed products or any of our product candidates that are approved in the future; failure to successfully conduct future clinical trials for our marketed products or our product candidates and our potential inability to enroll or retain sufficient patients to conduct and complete the trials or generate data necessary for regulatory approval of our product candidates or to permit the use of ARIKAYCE in the broader population of patients with MAC lung disease, among other things; development of unexpected safety or efficacy concerns related to our marketed products or our product candidates; risks that our clinical studies will be delayed, that serious side effects will be identified during drug development, or that any protocol amendments submitted will be rejected; failure to successfully predict the time and cost of development, regulatory approval and commercialization for novel gene therapy products; risk that interim, topline or preliminary data from our clinical trials that we announce or publish from time to time may change as more patient data become available or may be interpreted differently if additional data are disclosed, or that blinded data will not be predictive of unblinded data; risk that our competitors may obtain orphan drug exclusivity for a product that is essentially the same as a product we are developing for a particular indication; our inability to attract and retain key personnel or to effectively manage our growth; our inability to successfully integrate our acquisitions and appropriately manage the amount of management's time and attention devoted to integration activities; risks that our acquired technologies, products and product candidates will not be commercially successful; inability to adapt to our highly competitive and changing environment; inability to access, upgrade or expand our technology systems or difficulties in updating our existing technology or developing or implementing new technology; risk that we are unable to maintain our significant customers; risk that healthcare legislation or other government action materially adversely affects our business; business or economic disruptions due to catastrophes or other events, including natural disasters or public health crises; risk that our current and potential future use of AI and machine learning may not be successful; deterioration in general economic conditions in the U.S., Europe, Japan and globally, including the effect of prolonged periods of inflation, affecting us, our suppliers, third-party service providers and potential partners; risk that we could become involved in costly intellectual property disputes, be unable to adequately protect our intellectual property rights or prevent disclosure of our trade secrets and other proprietary information, and incur costs associated with litigation or other proceedings related to such matters; restrictions or other obligations imposed on us by agreements related to our marketed products or our product candidates, including our license agreements with PARI and AstraZeneca AB, and failure to comply with our obligations under such agreements; the cost and potential reputational damage resulting from litigation to which we are or may become a party, including product liability claims; risk that our operations are subject to a material disruption in the event of a cybersecurity attack or issue; changes in laws and regulations applicable to our business, including any pricing reform and laws that impact our ability to utilize certain third parties in the research, development or manufacture of our product candidates, and failure to comply with such laws and regulations; our history of operating losses, and the possibility that we never achieve or maintain profitability; goodwill impairment charges affecting our results of operations and financial condition; inability to repay our existing indebtedness and uncertainties with respect to our ability to access future capital; and delays in the execution of plans to build out an additional third-party manufacturing facility approved by the appropriate regulatory authorities and unexpected expenses associated with those plans.

Additional Disclaimers

Please be aware that TPIP, INS1201, INS1202, INS1148, and INS1033 are investigational products that have not been approved for sale or found safe or effective by the FDA or any regulatory authority. In addition, ARIKAYCE has not been approved for the treatment of all patients with MAC lung disease and brensocatib has not been approved for the treatment of patients with non-cystic fibrosis bronchiectasis outside the U.S. and the E.U. This presentation is not promotion or advertisement of ARIKAYCE, BRINSUPRI, TPIP, INS1201, INS1202, INS1148, or INS1033. Insmed, ARIKAYCE and BRINSUPRI are registered trademarks of Insmed Incorporated. All other trademarks are property of their respective owner(s).

Certain information contained in this presentation relates to or is based on studies, publications, surveys and other data obtained from third-party sources, as well as our own internal estimates and research. While we believe the information in these third-party sources to be reliable as of the date of this presentation, we have not independently verified any such information or the underlying assumptions relied on in such third-party sources. In addition, while we believe our internal research is reliable, such research has not been verified by any independent source.

Three Therapeutic Areas, One Goal:
Develop First- and Best-in-Class* Therapies

Research & Business Development

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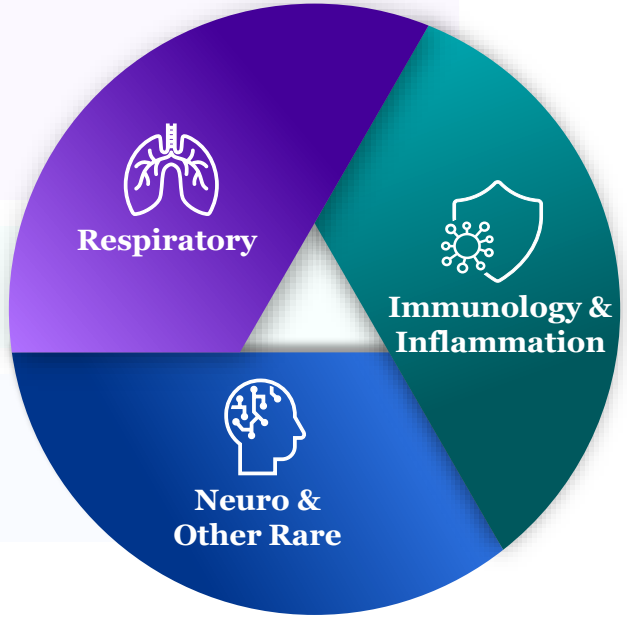
* “Best-in-disease/best-in-class" indicates a profile that could be considered more attractive than other treatment options for a particular disease. Head-to-head clinical trials are not anticipated.

First-in-Class and Potentially **Best-in-Class*** Assets Across Each Phase of Development

		Pre-Clinical	Phase 1	Phase 2	Phase 3	Commercial
RESPIRATORY	BRINSUPRI® (Brensocatib)**: Non-Cystic Fibrosis Bronchiectasis (NCFB)					
	ARIKAYCE® (Amikacin Liposome Inhalation Suspension): Refractory MAC Lung Disease					
	Amikacin Liposome Inhalation Suspension: MAC Lung Disease					
	TPIP: Pulmonary Hypertension Interstitial Lung Disease (PH-ILD)					
	TPIP: Pulmonary Arterial Hypertension (PAH)					
	TPIP: Progressive Pulmonary Fibrosis (PPF)					
	TPIP: Idiopathic Pulmonary Fibrosis (IPF)					
	INS1148, SCF248 mAb: Progressive Pulmonary Fibrosis (PPF)					
	INS1148, SCF248 mAb: Idiopathic Pulmonary Fibrosis (IPF)					
	INS1033: DPP1 Inhibitor: Chronic Obstructive Pulmonary Disease (COPD)					
I&I	INS1033, DPP1 Inhibitor: Rheumatoid Arthritis (RA)					
	INS1033, DPP1 Inhibitor: Ulcerative Colitis (UC)					
N&OR	INS1201, Gene Therapy: Duchenne Muscular Dystrophy (DMD)					
	INS1202, Gene Therapy: Amyotrophic Lateral Sclerosis (ALS)					
	INS1203, Gene Therapy: Stargardt Disease					



MAC / MACLD: *Mycobacterium avium* complex lung disease | TPIP: treprostinil palmitil inhalation powder | SCF248 mAb: stem cell factor 248 monoclonal antibody | DPP1: dipeptidyl peptidase 1 inhibitor | I&I: Immunology & Inflammation Therapeutic Area | N&OR: Neuro & Other Rare Therapeutic Area | U.S.: United States | UK: United Kingdom | * "Best-in-disease/best-in-class" indicates a profile that could be considered more attractive than other treatment options for a particular disease. Head-to-head clinical trials are not anticipated. | ** Brensocatib is approved in the U.S., Europe, and the UK. Brensocatib remains under review by regulatory authorities in Japan

Second-Quarter Performance Supports Updated Full-Year Guidance for BRINSUPRI

Full-Year 2026	Revenue GUIDANCE	Gross-to-Net GUIDANCE
Brinsupri® (brensocatib)	**$1.25B to $1.4B†** *Previously "Greater than $1B"*	**Mid-20%s to High-20%s** *Previously "Mid-20%s to Low-30%s"*
ARIKAYCE® (amikacin liposome inhalation suspension) Limited Population	**$450M to $470M‡** *Unchanged*	**Low-20%s to Mid-20%s** *Unchanged*

B: billion | M: million | † BRINSUPRI guidance does not contemplate meaningful revenue contribution from a potential Japanese approval in the second-half of 2026 | ‡ ARIKAYCE guidance does not contemplate contribution from a potential label expansion approval in the U.S. and Japan in 2026

Peak Revenue Estimate **Raised to $14B+** for Three Lead Assets Across Their Respective Indications*

	Prior	***Updated***
Brinsupri®	$5B+ *Bronchiectasis*	$7B+ *Bronchiectasis†*
TPIP *(Investigational Product)*	$2B+ *PAH & PH-ILD Only*	$6B+ *PAH, PH-ILD, PPF, IPF*
ARIKAYCE®	$1B+ *All MACLD*	$1B+ *All MACLD*

Total Peak Revenue Estimate*

$14B+

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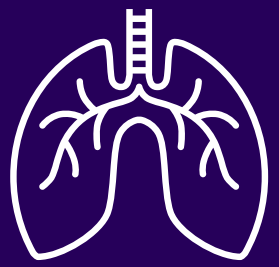
B: billion | NCFB / Bronchiectasis: non-cystic fibrosis bronchiectasis | TPIP: treprostinil palmitil inhalation powder | PAH: pulmonary arterial hypertension | PH-ILD: pulmonary hypertension due to interstitial lung disease | PPF: progressive pulmonary fibrosis | IPF: idiopathic pulmonary fibrosis | MAC / MACLD: *Mycobacterium avium* complex lung disease | COPD: chronic obstructive pulmonary disease | FDA: Food and Drug Administration | * Assumes approval in listed indications by applicable regulatory authorities | † Updated estimate reflects expected growth of the currently addressable NCFB market, driven by earlier and more consistent diagnosis and exacerbation tracking due to increased awareness among physicians and patients. This estimate does not include contributions from the potentially meaningful opportunity of NCFB patients from the comorbid COPD and asthma populations | Note: TPIP is an investigational product that has not been approved for sale or found safe or effective by the FDA or any regulatory authority



Respiratory

THERAPEUTIC AREA

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Brinsupri®
(brensocatib)

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BRINSUPRI Approved by the FDA

- Approved in **10 mg** and **25 mg** tablet form for **adults** and **adolescents** 12+ years with NCFB
- Indication label has **no requirement** on number of documented pulmonary exacerbations
- **25 mg** dose label includes details on statistically significant **benefits on FEV_1**
- Label reflective of the **safety profile** observed during clinical development

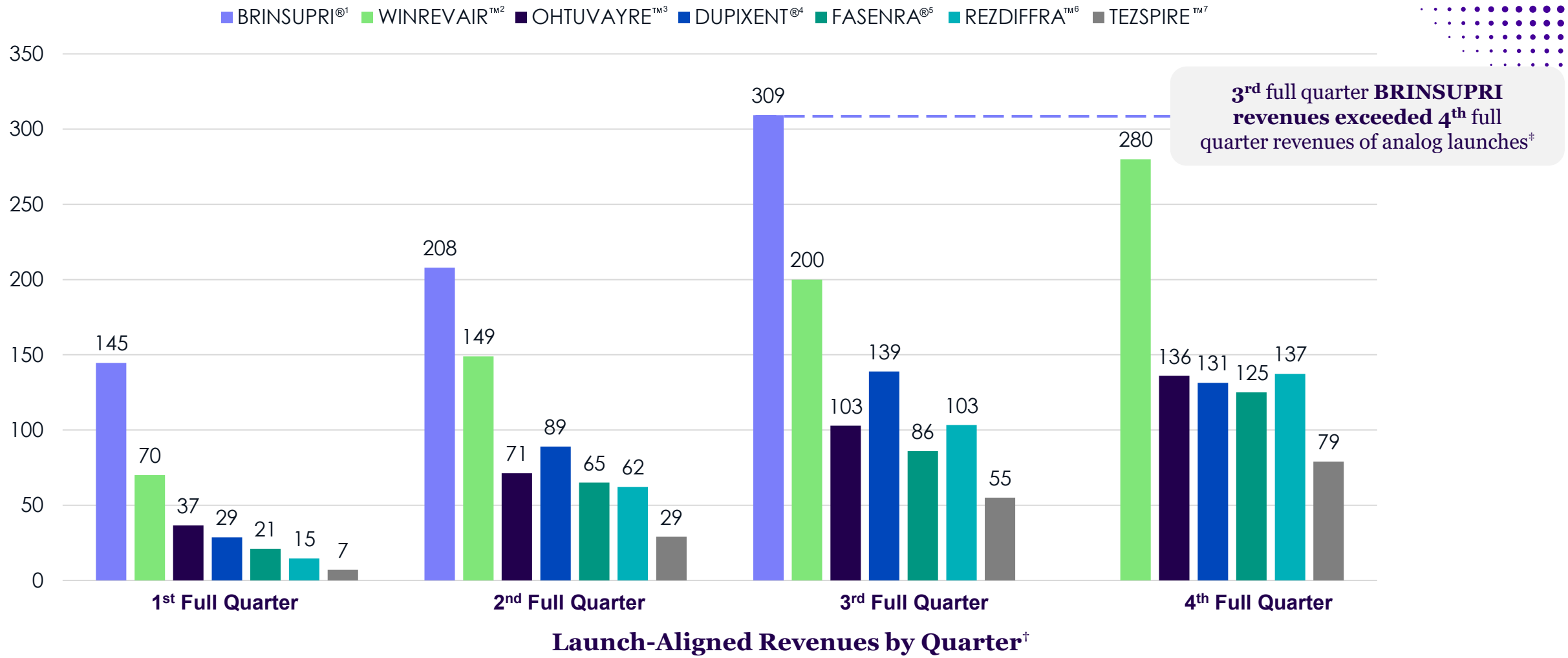
Label Offers Physicians Flexibility to Prescribe Either Dose of BRINSUPRI to Patients

FDA approval received August 12, 2025 | NCFB / Bronchiectasis: non-cystic fibrosis bronchiectasis | FEV_1: forced expiratory volume in 1 second (a key measure of lung function) | mg: milligram

Strong Second-Quarter Revenue Results Increase Confidence to **Raise Full-Year 2026 Guidance**

M: million | B: billion | Q: quarter | † Unaudited revenues for three months ended June 30, 2026

Third Full-Quarter Revenues Continue to Outperform Analogs, Enabled by Operational Excellence



Launch-Aligned Revenues by Quarter†

U.S.: United States | † Launch-aligned revenues compare each product based on quarters since launch (1st quarter post-launch, 2nd quarter post-launch, etc.), regardless of calendar quarter or year. All reported revenues are in millions of U.S. dollars. | ‡ Includes the launch-aligned revenues for analog launches in each launch's fourth full quarter on the market | Note: unaudited BRINSUPRI revenues for the first and second quarters of 2026 | Note: Numbered footnotes referenced on this slide can be found in the appendix of this presentation titled "Launch Analog Footnotes" | Note: Product revenues are reported in U.S. dollars and sourced from financial filings and earnings disclosures as described in more detail in the footnotes. Revenues have not been adjusted for inflation and reflect reported values as of the date of public disclosure.

Strategic Collaborations and **Future Studies** Aim to Expand Long-Term Evidence

European Multi-centre Bronchiectasis Audit and Research Collaboration (EMBARC)

3-year open-label study

Up to 3,000 patients

Across six countries

Study Goals:

- Assess **long-term disease modification** potential with sustained 25 mg brensocatib treatment
- Evaluate whether **earlier brensocatib initiation** further slows disease progression

Brinsupri®

Ongoing plans to demonstrate long-term evidence through Phase 4 and real-world studies in the U.S. that reinforce BRINSUPRI's leadership in NCFB

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EMBARC: European Multi-centre Bronchiectasis Audit and Research Collaboration (European bronchiectasis registry) | mg: milligram | U.S.: United States | NCFB: non-cystic fibrosis bronchiectasis

Brensocatib in **Bronchiectasis** Opportunity Could Potentially Reach >1M Patients*

Brinsupri® (brensocatib)

Diagnosed with Bronchiectasis[1]	500K	600K	150K
Undiagnosed‡ Bronchiectasis[2]	2.4M	2.1M	0.8M
Asthma or COPD[3]	32M	27M	17M

TAM: total addressable market | U.S.: United States | *Pending regulatory approval for bronchiectasis indication in specified regions | NCFB / Bronchiectasis: non-cystic fibrosis bronchiectasis | M: million | K: thousand | † EU_5 comprised of France, Germany, Italy, Spain and the United Kingdom (UK) | ‡ Includes misdiagnosed, miscoded, and undiagnosed NCFB patients | Note: COPD and asthma patients may be comorbid with bronchiectasis and not all patients with bronchiectasis have comorbid asthma or COPD | Note: Numbered prevalence footnotes referenced on this slide can be found in the appendix of this presentation titled “Epidemiological Footnotes”

ARIKAYCE®
(amikacin liposome inhalation suspension)

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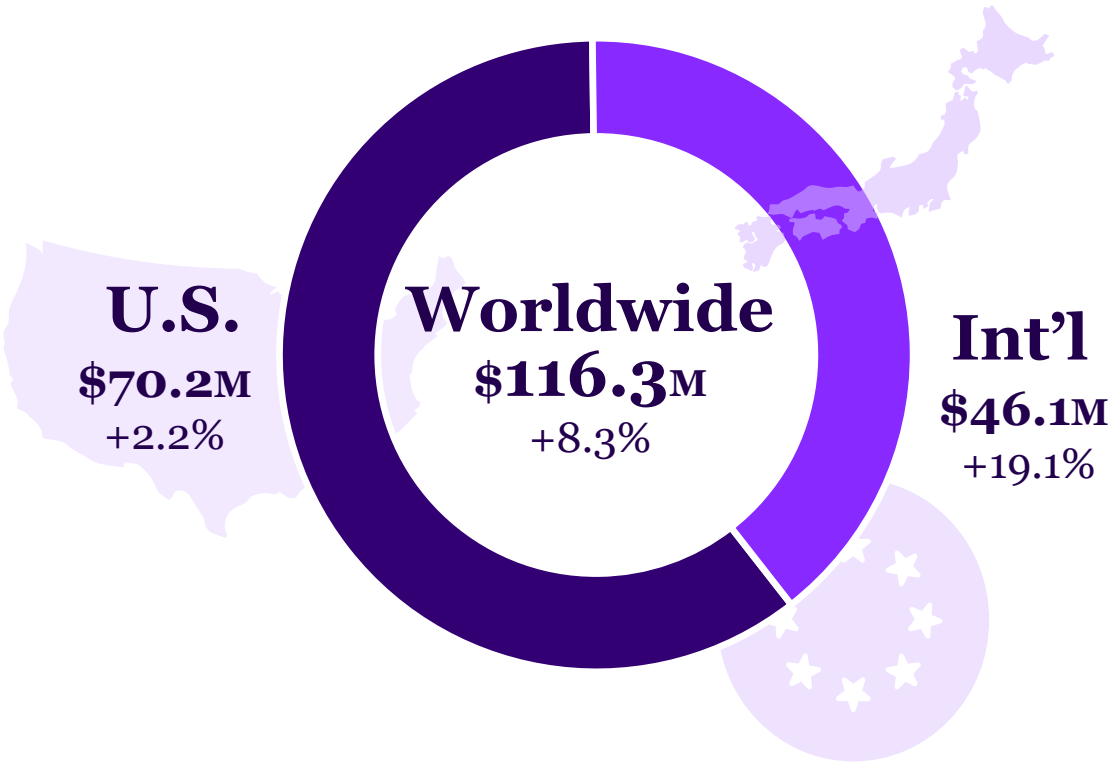
Executing Commercially While Preparing for Label Expansion in the U.S. & Japan*

Q2 2026 Revenue†



Preparing for Potential Label Expansion

- ✓ **Filed sNDA** with **FDA** in July in newly diagnosed MACLD patients
  - ► *U.S. label expansion would extend ARIKAYCE treatment to **all MACLD** patients, if approved*
- Intend to **submit data to PMDA in 2H:26** to support potential Japanese label expansion
- Demonstrated **clinical evidence** and an **experienced commercial team** position ARIKAYCE for launch success*

U.S.: United States | Int'l: international | M: million | sNDA: supplemental new drug application | FDA: Food and Drug Administration | PMDA: Pharmaceuticals and Medical Devices Agency | H: half | MACLD: *Mycobacterium avium* complex lung disease | * if expanded label for ARIKAYCE is approved in the U.S. and Japan | † Unaudited revenues for three months ended June 30, 2026; Growth is vs. same prior year period

ARIKAYCE Has Potential to Be the Best-in-MACLD Treatment

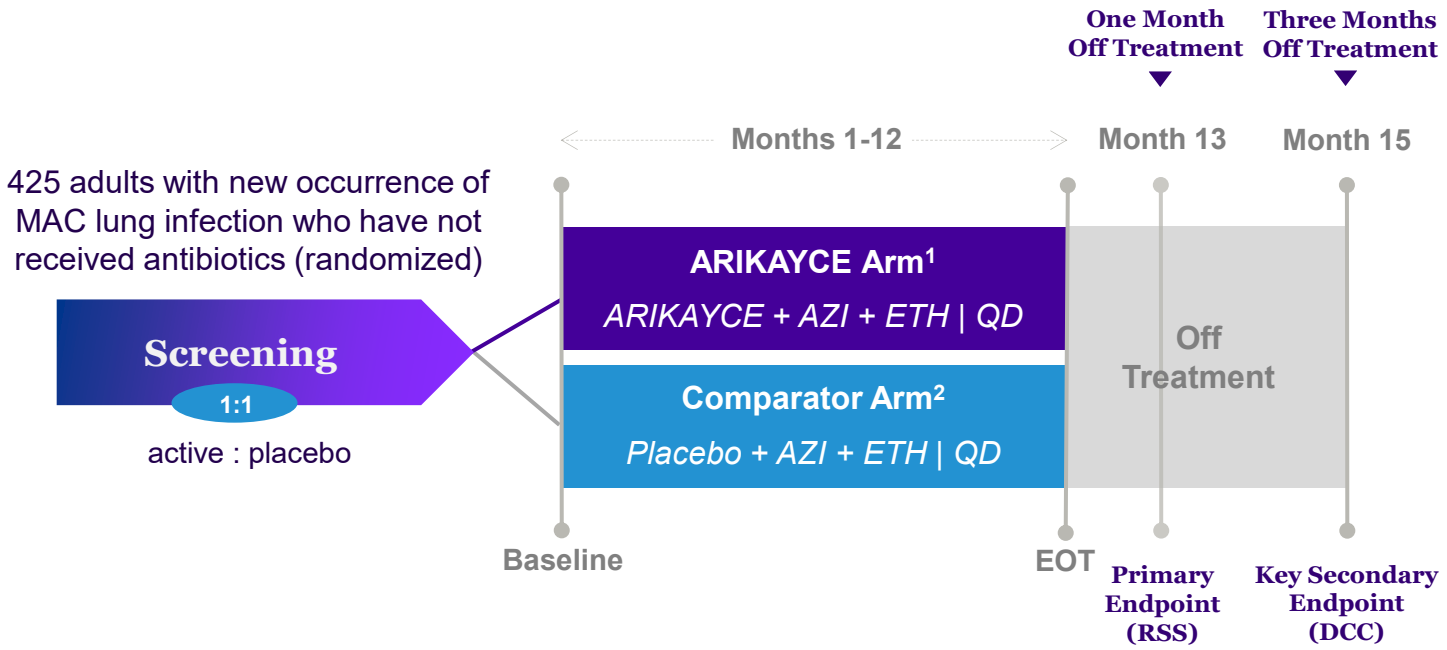
ARIKAYCE® (amikacin liposome inhalation suspension) | Limited Population

Refractory MAC[4]	**12-17K**	**1.4K**	**15-18K**
MACLD[4]	**95-115K**	**14K**	**125-145K**

We anticipate marketing ARIKAYCE in newly diagnosed MACLD patients at same price and dosage as currently available ARIKAYCE, if approved*

U.S.: United States | TAM: total addressable market | MAC / MACLD: *Mycobacterium avium* complex lung disease; Refractory MAC patients included in all MACLD TAM estimates | K: thousand | * If approved | † EU_5 comprised of France, Germany, Italy, Spain and the United Kingdom (UK) | Note: Numbered prevalence footnotes referenced on this slide can be found in the appendix of this presentation titled "Epidemiological Footnotes"

ARIKAYCE Phase 3b in MACLD: ENCORE



ENCORE

Primary Endpoint

- Change from **baseline in Respiratory Symptom Score (RSS)**[3] at Month 13 (one month off treatment)

Multiplicity-Controlled Secondary Endpoints*

- Proportion of patients achieving culture conversion by Month 13 (one month off treatment)
- Proportion of patients achieving **durable culture conversion** by Month 15 (three months off treatment)
- Proportion of patients achieving culture conversion by Months 12 and Month 6
- Change from baseline fatigue symptom score at Month 13 (PROMIS Fatigue T-score)

Other Secondary & Exploratory Endpoints

- Change from **baseline in RSS** at Month 15
- Proportion of participants meeting the **meaningful within-patient change** (MWPC) threshold as reflected in the change in RSS computed from baseline to Month 13
- Time to culture conversion

MAC / MACLD: *Mycobacterium avium* complex lung disease | AZI: Azithromycin | ETH: Ethambutol | EOT: end of treatment | QD: once-daily | U.S.: United States | DCC: durable culture conversion | * A predefined sequential testing approach was applied to control the overall type I error rate (α=0.05) | [1] ARIKAYCE (590 mg) + macrolide-based background regimen consisting of AZI (250 mg) and ETH (15 mg/kg) | [2] Empty liposome control placebo + macrolide-based background regimen consisting of AZI and ETH | [3] Respiratory Symptom Score (RSS) ranges from 0 to 100, with positive change indicating improvement | Culture conversion was defined as no MAC growth on agar and broth media in all sputum cultures at 2 consecutive visits (8 total samples). Durable culture conversion defined as no MAC growth (culture negative) at Months 11, 12, 13, and 15

Results Show That Early Treatment With **ARIKAYCE** + Multidrug Therapy Can Significantly Improve Outcomes for MACLD Patients

Treatment with ARIKAYCE[1] vs. Comparator[2] showed…

RSS Improvement

- ✓ **Statistically significant** at Month 13*
- ✓ **Strengthening of improvement** at Month 15^
- ✓ **Greater proportion** of clinically meaningful **RSS responders** at Month 13

Culture Conversion

- ✓ **Statistically significant greater conversion** by Months 6, 12, 13 and 15*
- ✓ **Earlier, greater,** and **more durable** conversion

Safety & Tolerability

- ✓ >90% completion in both study arms
- ✓ No new or unexpected safety signals observed

AZI: Azithromycin | ETH: Ethambutol | [1] ARIKAYCE (590 mg) + macrolide-based background regimen consisting of AZI (250 mg) and ETH (15 mg/kg) | [2] Empty liposome control placebo + macrolide-based background regimen consisting of AZI and ETH | MAC / MACLD: *Mycobacterium avium* complex lung disease | RSS: Respiratory Symptom Score | * statistically significant | ^ not multiplicity controlled; nominally statistically significant

Treprostinil Palmitil Inhalation Powder (TPIP)

TPIP: treprostinil palmitil inhalation powder | FDA: Food and Drug Administration | Note: TPIP is an investigational product that has not been approved for sale or found safe or effective by the FDA or any regulatory authority

Investigational Once-Daily Prostanoid With the Potential to Deliver Best-in-Class† Efficacy With Enhanced Tolerability

Potential Advantages of TPIP

Efficacy*

- **Inhaled therapy** delivered directly to the lung tissue
- **Slow-release** properties enable **high, consistent** treprostinil levels in lungs
- **Flexibility to titrate up** to patient max tolerated dose in pursuit of optimal therapeutic benefit

Safety*

- Potential for **reduced systemic side effects** due to lower peak exposure
- Inert pro-drug formula may **improve tolerability**
  - Shown preclinically to **reduce cough** vs. active drug of the same dose

Convenience**

- Administered **once daily** vs. the 4-times per day of other approved inhaled treprostinils
  - **1-2 breaths per day** (even for 1,280 µg dose)
- Less frequent dosing may improve **patient adherence** to therapy

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TPIP: treprostinil palmitil inhalation powder | PAH: pulmonary arterial hypertension | PH-ILD: pulmonary hypertension due to interstitial lung disease | * Analysis based on safety and tolerability data from the Phase 2a PH-ILD published May 2024, and the Phase 2b PAH study published June 2025 | ** No head-to-head or convenience studies have been conducted or planned | † "Best-in-disease/best-in-class" indicates a profile that could be considered more attractive than other treatment options for a particular disease. Head-to-head clinical trials are not anticipated.

Four TPIP Indications Represent Substantial Commercial Opportunities

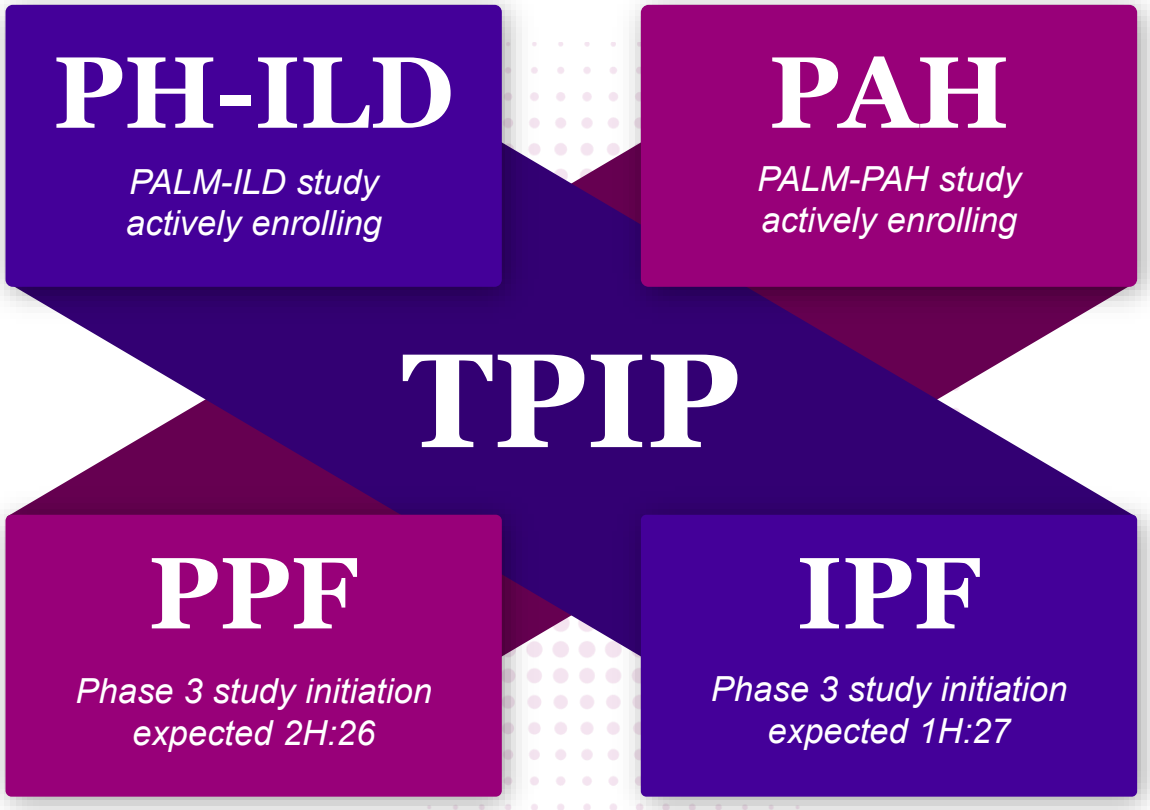
~$300K

U.S. Pricing Benchmark | TYVASO DPI® List Price‡

TPIP	U.S. TAM	EU5† TAM	Japan TAM
PAH[5]	35K	40K	15K
PH-ILD[6]	50K	65K	20K
PPF[7]	145K	90K	20K
IPF[8]	125K	75K	20K

TPIP: treprostinil palmitil inhalation powder | TAM: total addressable market | IPF: idiopathic pulmonary fibrosis | PPF: progressive pulmonary fibrosis | PH-ILD: pulmonary hypertension due to interstitial lung disease | PAH: pulmonary arterial hypertension | U.S.: United States | K: thousand | DPI: dry powder inhalation | † EU_5 comprised of France, Germany, Italy, Spain and the United Kingdom (UK) | ‡ Wholesale acquisition cost (WAC) as of March 12, 2024 | Note: IPF and PPF estimates do not account for overlap with PH-ILD; estimated that ~10% of IPF and PPF patients may overlap with PH-ILD | Note: Numbered prevalence footnotes referenced on this slide can be found in the appendix of this presentation titled “Epidemiological Footnotes”

Expansive Registrational Program Across **Four Indications** Progressing on Track



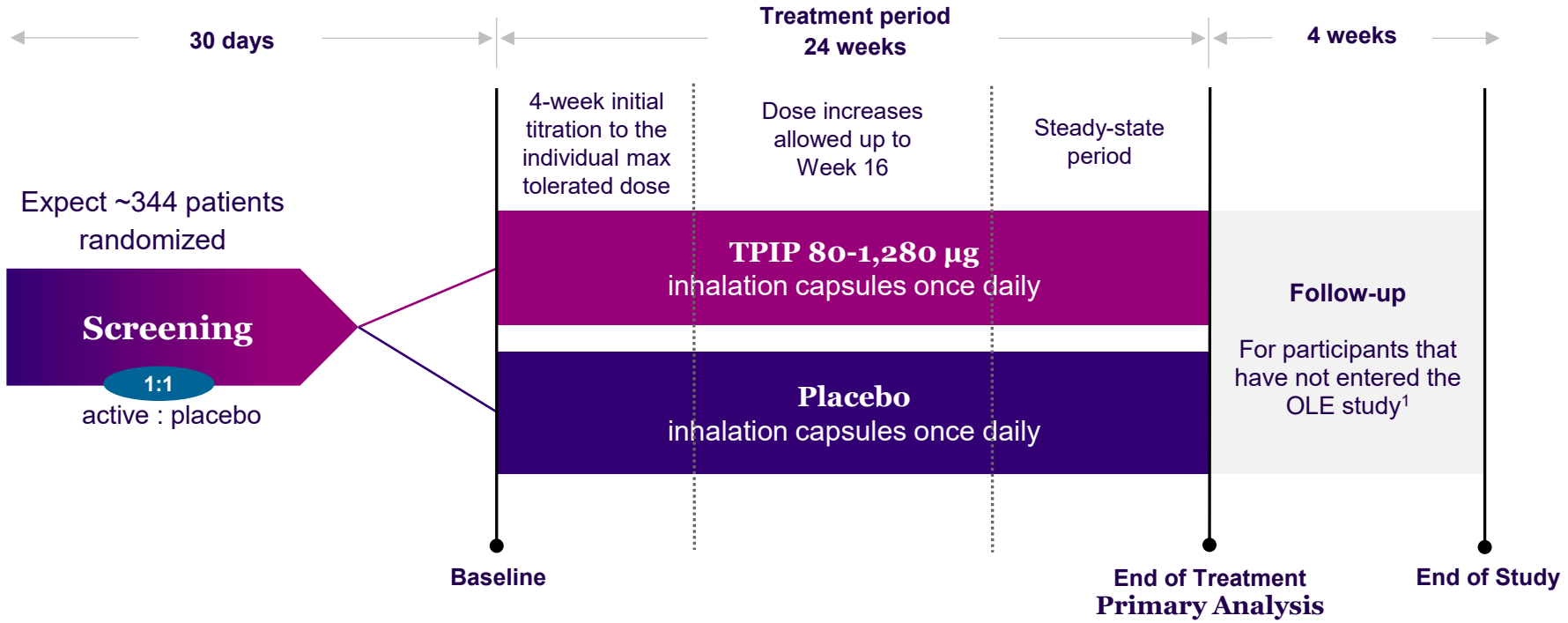
All Phase 3 studies permit titration to patient ***maximum tolerated dose*** *(up to 1,280 µg)*

- TPIP's **broad dosing range** could provide physicians with the **flexibility** to optimize the balance between **efficacy** and **tolerability**
- The flexibility to **quickly** & **safely** dose TPIP to **higher levels** than other inhaled TRE therapies could **meaningfully differentiate** it within the class
  - *The ability to continue to dose patients higher on inhaled therapy* ***could delay their need to switch to parenteral options***

TPIP: treprostinil palmitil inhalation powder | TRE: treprostinil | PAH: pulmonary arterial hypertension | PH-ILD: pulmonary hypertension due to interstitial lung disease | PPF: progressive pulmonary fibrosis | IPF: idiopathic pulmonary fibrosis | µg: micrograms | Note: Initiation indicates that trial sites are open and ready to screen patients for enrollment

TPIP Phase 3 in PH-ILD: PALM-ILD

NCT07179380 Trial summary



PALM-ILD (Week 24)

Primary Endpoint

- Change in baseline exercise capacity (6MWD) at peak exposure (1-3 hours post-dose)

Secondary Endpoints

- Time to clinical worsening[2]
- Time to first major morbidity or mortality[3]
- Change in baseline cardiac stress (NT-proBNP concentration)
- Change in baseline 6MWD at trough exposure (pre-dose) at Week 22
- Mean change from baseline in living with pulmonary fibrosis (L-PF) total symptom domain score
- Pharmacokinetics

Exploratory Endpoints

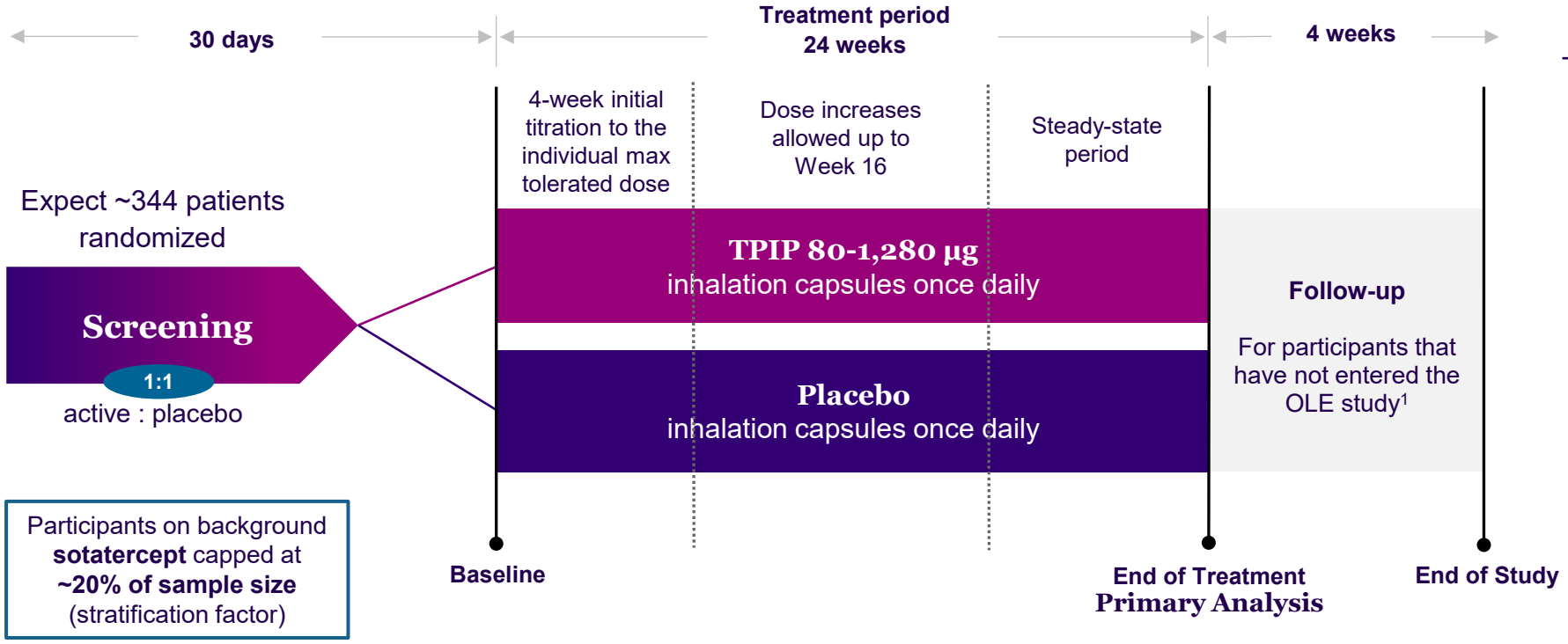
- ILD exacerbations
- Change from baseline in Quality of Life (QoL)
- Change from baseline lung function (FVC, FEV_1)
- Respiratory imaging

Measured at Week 24 unless otherwise specified

TPIP: treprostinil palmitil inhalation powder | PH-ILD: pulmonary hypertension due to interstitial lung disease (ILD) | 6MWD: 6-minute walk distance | OLE: open-label extension | NT-proBNP: N-terminal pro-B-type natriuretic peptide | FVC: forced vital capacity | FEV_1: forced expiratory volume in 1 second (a key measure of lung function) | WHO: World Health Organization | NYHA: New York Heart Association | [1] Participants enrolled in the OLE study will remain on-treatment until Week 104, followed by a 4-week follow-up | [2] Clinical worsening is defined as one of the following: (1) hospitalization due to cardiopulmonary indication related to PH-ILD, (2) deterioration of PH-ILD, including a decrease of 15% or more in 6MWD and/or signs and symptoms of worsened right heart failure or WHO/NYHA functional class, (3) lung transplantation (except pre-planned prior to study), (4) death from any cause. All events will be adjudicated by an independent blinded committee. | [3] Morbidity or mortality defined as one of the following: (1) hospitalization due to cardiopulmonary indication related to the worsening of PH-ILD, (2) lung transplantation (except pre-planned prior to study), (3) death from any cause.

TPIP Phase 3 in PAH: PALM-PAH

NCT07481981 Trial summary



PALM-PAH (Week 24)

Primary Endpoint

- Change in baseline exercise capacity (6MWD) at peak exposure (1-3 hours post-dose)

Secondary Endpoints

- Proportion of patients with baseline WHO FC improvement
- Change in baseline 6MWD at trough exposure (pre-dose) at Week 22
- Change in baseline cardiac stress (NT-proBNP concentration)
- Change in baseline PAH-SYMPACT domain scores
- Time to clinical worsening[2]

Exploratory Endpoints

- Change from baseline in Quality of Life (QoL)
- Plasma concentrations of treprostinil palmitil and treprostinil over time
- Safety & tolerability[3]

Measured at Week 24 unless otherwise specified

TPIP: treprostinil palmitil inhalation powder | PAH: pulmonary arterial hypertension | 6MWD: 6-minute walk distance | OLE: open-label extension | NT-proBNP: N-terminal pro-B-type natriuretic peptide | WHO: World Health Organization | NYHA: New York Heart Association | FC: functional class | [1] Participants enrolled in the OLE study will remain on-treatment until Week 104, followed by a 4-week follow-up | [2] Clinical worsening is defined as one of the following: (1) death from any cause,(2) hospitalization for worsening of PAH (≥24 hours), (3) need for atrial septostomy, (4) worsening-related listing for lung and/or heart-lung transplant, (5) need to initiate parenteral therapy with an approved PAH therapy, or (6) deterioration of PAH (defined as a combination of the following changes from baseline: a decrease in 6MWD of ≥15%, confirmed by 2 tests ≥4 hours but not >2 weeks apart, and signs/symptoms of worsened right heart failure or worsened WHO/NYHA FC). All events will be adjudicated by an independent blinded committee. | [3] including AEs, laboratory assessments, vital signs, and 12-lead electrocardiogram

Positive OLE Study Results in PAH Reinforce TPIP's Potential to Become the **Prostanoid of Choice**

Phase 2b Study Results

PVR Reduction[1]	~35%*
6MWD Improvement[2] (meters)	+35·5^
NT-proBNP Reduction[3]	~60%^

Placebo-Adjusted Efficacy Results Measured at Week 16 (~24 Hours After Dose)

12-Month Data from Ongoing OLE Study‡

6MWD Improvement[4] (meters)	+55†
NT-proBNP Reduction[5]	~60%†
WHO FC I or II Achievement[6]	~80%
REVEAL Lite 2.0: *Refined Low Risk* Status Achievement[7]	~65%

Results Evaluated Against the Lead-in Study Baseline and Measured ~24 Hours After Dose for Applicable Measures (Not Placebo-Adjusted)

TPIP: treprostinil palmitil inhalation powder | PAH: pulmonary arterial hypertension | PVR: pulmonary vascular resistance | 6MWD: 6-minute walk distance | NT-proBNP: N-terminal pro-B-type natriuretic peptide, a biomarker for cardiac stress (concentration levels) | WHO: World Health Organization | FC: functional class | OLE: open-label extension | The REVEAL Lite 2.0 risk calculator is a simplified, non-invasive medical tool used to estimate the mortality and disease progression risk for adult patients with PAH | * Highly statistically significant | ^ Nominally statistically significant; not adjusted for multiplicity | † Metric measured ~24 hours after prior dose was administered and evaluated against the Phase 2b lead-in study pre-randomization baseline value | ‡ Includes all OLE patients in both the "Continued TPIP" and "Placebo Crossed" treatment groups | Note: Numbered footnotes referenced on this slide can be found in the appendix of this presentation

FDA Grants Treprostinil Palmitil **Orphan Drug Designation** in PAH

Efficacy

Placebo-Adjusted Improvement in 6MWD † at Week 16[1]

+35.5 *

meters

*** Nominally statistically significant in Phase 2**

Potential Clinical Superiority

vs. same drugs already approved for PAH

Major Contribution to Patient Care

TPIP Profile

Once-daily therapy with:

- ✓ **continuity** of parenteral treatment
- ✓ **localization** of inhaled therapy

PAH: pulmonary arterial hypertension | FDA: Food and Drug Administration | TPIP: treprostinil palmitil inhalation powder | * Nominal p-value not adjusted for multiplicity | † Covariate-adjusted estimate of location shift. Analysis performed using a rank ANCOVA model, adjusting for treatment group, baseline 6-minute walk distance (6MWD), and randomization stratification factors | [1] Measured ~24 hours after dose

TPIP's Profile Could Represent a Compelling Option in the Evolving PAH Treatment Landscape

TPIP

Investigational product that has not been approved for sale or found safe or effective by the FDA or any regulatory authority

	RCT (16 weeks)	OLE (12 months)	
	Phase 2b (Lead-in)	*Continued Treatment*	*Placebo Crossed*
PVR	-35%[1]	N/A	N/A
6MWD (meters)	+35.5[2]	+55.7[4] *vs. lead-in baseline*	+54.1[4] *vs. lead-in baseline*
NT-proBNP (pg/mL)	-60%[3]	-60%[5] *vs. lead-in baseline*	-60%[5] *vs. lead-in baseline*
Functional Class	30% of patients on treatment improved WHO FC[8]	~80% of OLE patients achieved FC I or II[6]	

TYVASO (treprostinil) INHALATION SOLUTION

	RCT (12 weeks)	OLE (12 months)	
	Phase 3 TRIUMPH (Lead-in)	*Continued Treatment*	*Placebo Crossed*
PVR	N/A	N/A	N/A
6MWD (meters)	+20[9]	+38[10] *vs. lead-in baseline*	+25[10] *vs. lead-in baseline*
NT-proBNP (pg/mL)	-187[11]	N/A	N/A
Functional Class	No difference in NYHA FC between groups[12]	N/A	N/A

WINREVAIR™ (sotatercept-csrk) for injection 45 mg, 60 mg

	RCT (24 weeks)	OLE (SOTERIA) (12 months)[13]	
	*Ph2 PULSAR** or Ph3 STELLAR (Lead-ins)[13]*	*Continued Treatment*	*Placebo Crossed*
PVR	-34%** (0.7 mg dose)[14]	N/A	N/A
6MWD (meters)	+41[15]	-1.7[16] *vs. OLE baseline**	+47[16] *vs. OLE baseline**
NT-proBNP (pg/mL)	-442[17]	-33[18] *vs. OLE baseline**	-827[18] *vs. OLE baseline**
Functional Class	29% of patients on treatment improved WHO FC[19]	≥80% of OLE patients achieved FC I or II[20]	

RCT: randomized clinical trial | PAH: pulmonary arterial hypertension | TPIP: treprostinil palmitil inhalation powder | 6MWD: 6-minute walk distance | OLE: open-label extension | NYHA: New York Heart Association | FC: functional class | NT-proBNP: N-terminal pro-B-type natriuretic peptide | Ph: phase | PVR: pulmonary vascular resistance | WHO: World Health Organization | m: meters | pg/mL: picograms per milliliter | FDA: Food and Drug Administration | * Baseline is the measurement at Visit 1 of SOTERIA or the last measure from the parent study before rollover | **Phase 2 PULSAR data for PVR is included because it represents the largest reduction in PVR achieved by sotatercept in a published randomized placebo-controlled clinical trial | Note: A lead-in study may also be referred to as a parent study in different OLE designs | Note: Cross-trial comparisons are inherently limited and should be interpreted with caution. Differences in study design, patient populations, and prespecified statistical analysis plans may affect comparability. | Note: Numbered footnotes referenced on this slide can be found in the appendix of this presentation titled "TPIP Footnotes" | Note: TYVASO and WINREVAIR are trademarks of their respective owners

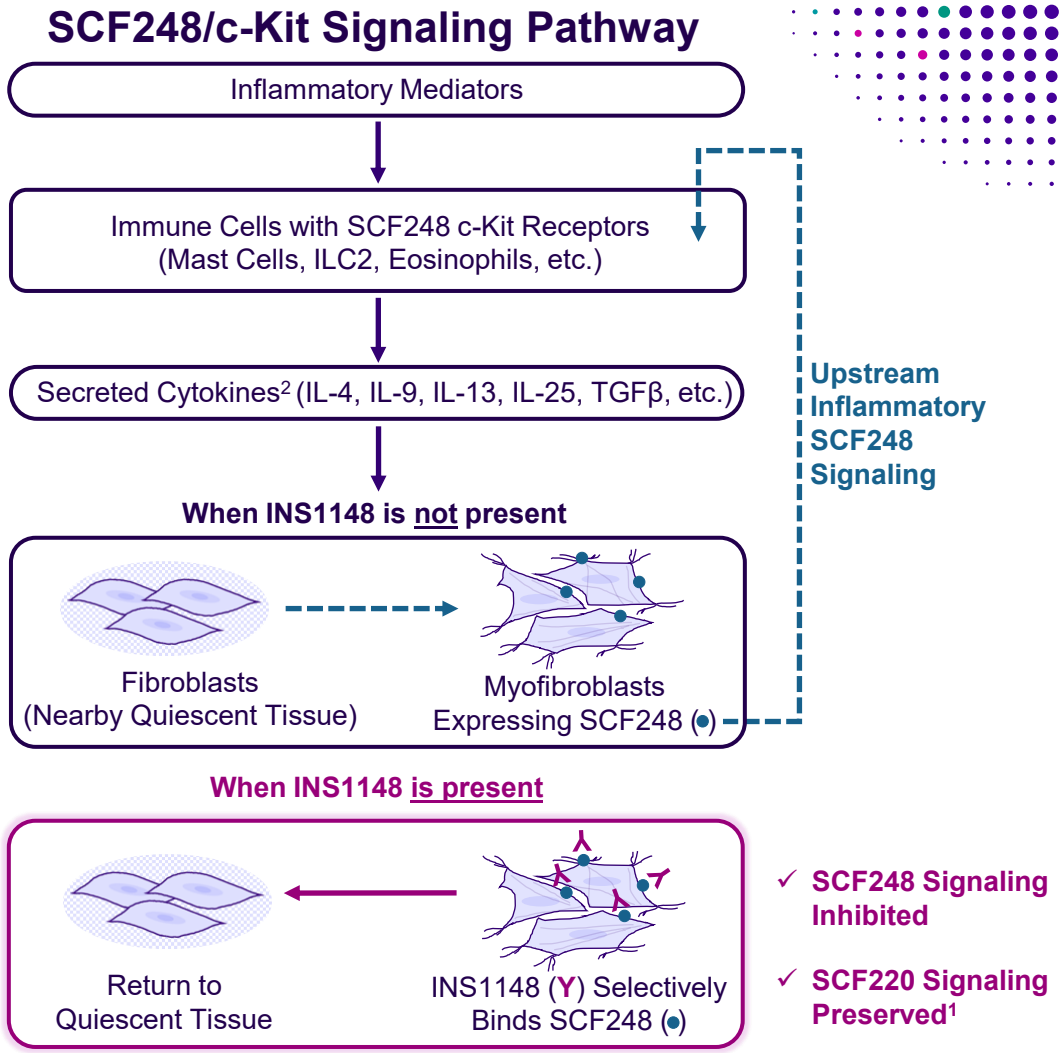
INS1148

INS1148: Potential First-in-Class Therapy for Respiratory and I&I Diseases

INS1148* is designed to selectively target SCF248, a specific isoform of SCF (c-Kit receptor ligand[1])

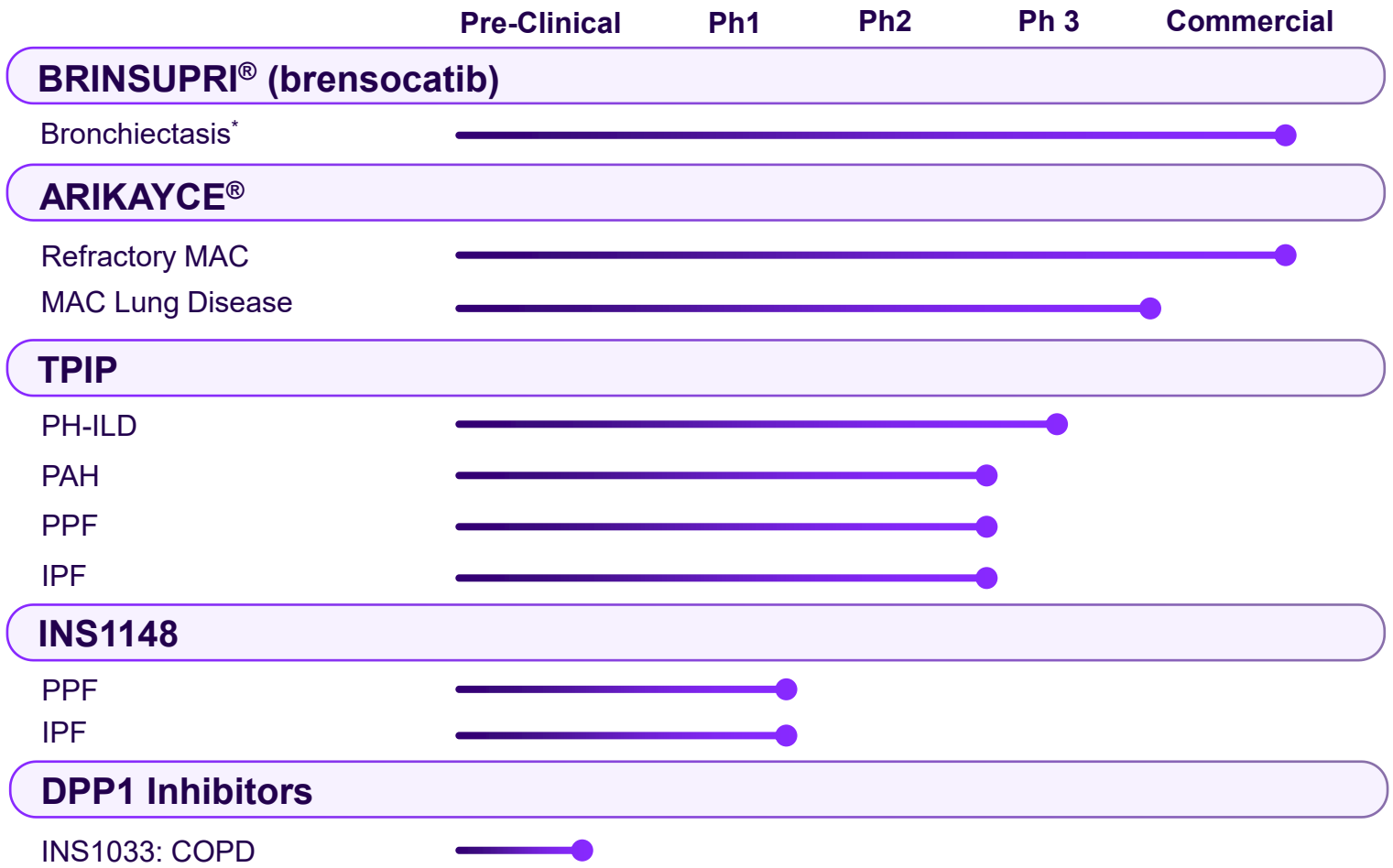
- ✓ **Inhibits** upstream SCF248/c-Kit signaling associated with **inflammatory diseases**
- ✓ **Preserves** homeostatic & tissue healing pathways associated with **SCF220[1]**

Plan to initiate Phase 2 programs in PPF and IPF



c-Kit: critical receptor tyrosine kinase protein on cell surfaces; binding site to SCF to trigger growth signals | IL: interleukin; cell signaling cytokines | TGFβ: transforming growth factor-beta; cytokine regulating cell growth, differentiation and tissue homeostasis | PPF: progressive pulmonary fibrosis | IPF: idiopathic pulmonary fibrosis | * Humanized monoclonal antibody | [1]SCF is the only known ligand for the c-Kit receptor with two known splice variants: SCF220 and SCF248. SCF220 is ubiquitously expressed and exerts its biological function as a transmembrane dimer that binds to c-Kit to signal homeostatic & tissue healing pathways | [2] Cytokines with the ability to promote inflammation, tissue remodeling, and fibrosis when upregulated | SCF: stem cell factor | I&I: immunological & inflammatory | ILC2: Group 2 innate lymphoid cells that produce different cytokines to direct immune responses

Respiratory Therapeutic Area Portfolio & Pipeline



Anticipated Catalysts

2H:26 | ARIKAYCE: Review ENCORE data with PMDA

2H:26 | BRINSUPRI: Japanese regulatory decision*

2H:26 | PALM-PPF: Ph3 trial initiation

1H:27 | PALM-IPF: Ph3 trial initiation

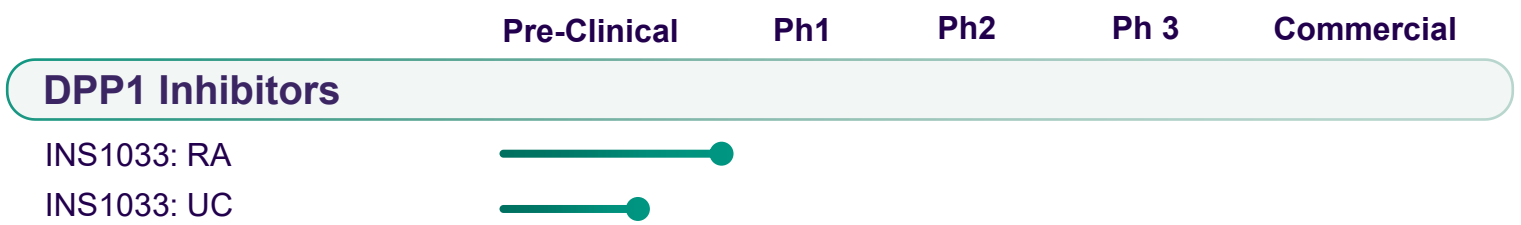
NCFB / Bronchiectasis: non-cystic fibrosis bronchiectasis | MAC / MACLD: *Mycobacterium avium* complex lung disease | TPIP: treprostinil palmitil inhalation powder | PH-ILD: pulmonary hypertension due to interstitial lung disease | PAH: pulmonary arterial hypertension | PPF: progressive pulmonary fibrosis | IPF: idiopathic pulmonary fibrosis | COPD: chronic obstructive pulmonary disease | FDA: Food and Drug Administration | PMDA: Pharmaceuticals and Medical Devices Agency | U.S.: United States | H: half | Ph: phase | * Brensocatib is approved in the U.S., Europe, and UK. Brensocatib remains under review by regulatory authorities in Japan | Initiation indicates that trial sites are open and ready to screen participants for enrollment

Immunology & Inflammation

THERAPEUTIC AREA

insmed®

Immunology & Inflammation Therapeutic Area Pipeline



Anticipated Catalysts

Q3:26 | RA: Ph1 study initiation in healthy volunteers

RA: rheumatoid arthritis | UC: ulcerative colitis | Q: quarter | Ph: phase | Initiation indicates that trial sites are open and ready to screen participants for enrollment

Neuro & Other Rare

THERAPEUTIC AREA

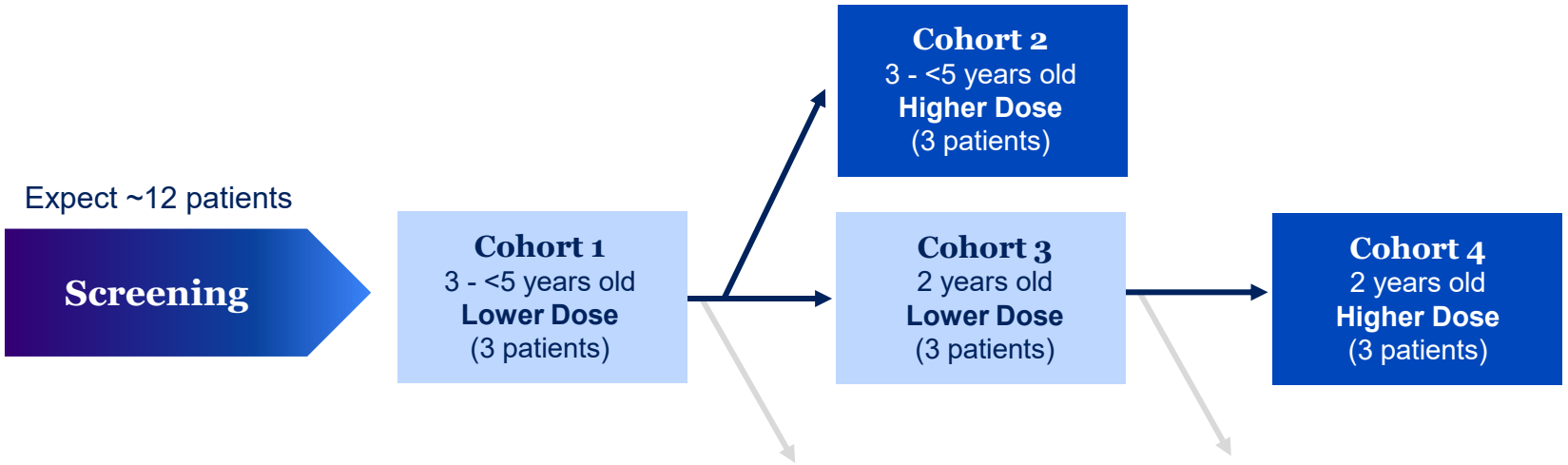
insmed®

INS1201 Phase 1 in DMD: ASCEND

NCT06817382 Trial summary

Key Trial Information

- Patients must be ambulatory at time of screening
- Single dose via intrathecal administration



The IDMC will meet **after the completion of the 30-day safety period** for the last participant in **Cohorts 1** and **Cohort 3** for a safety review **before initiating** to Cohort 2 and Cohort 4

ASCEND

Primary Endpoint

- Safety and tolerability (up to Week 96)

Secondary Endpoints

- Muscle dystrophin levels (DNA and protein expression) measured by ddPCR and quantitative protein analysis (Week 16 & 48)

Exploratory Endpoints

- Multiple age-appropriate functional and developmental outcomes

IDMC: Independent Data Monitoring Committee | ddPCR: droplet digital polymerase chain reaction | DNA: deoxyribonucleic acid | DMD: Duchenne muscular dystrophy

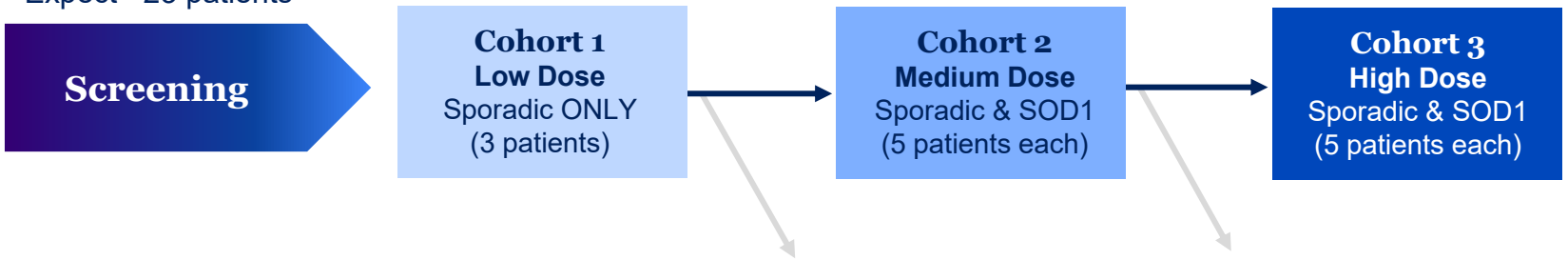
INS1202 Phase 1 in ALS: ARMOR

NCT07290062 Trial summary

Key Trial Information

- Cohort enrollment will be staggered, with a 30-day safety observation between the first 3 participants in a cohort regardless of ALS subpopulation
- ALS subtypes in Cohorts 2 and 3 can enroll in parallel contingent upon full enrolment of the prior cohort
- Single dose via intrathecal administration

Expect ~23 patients



The IDMC will meet **after the completion of the 30-day safety period** required between dosing the **last participant** at a given **dose level** and the **first participant** at the **subsequent dose level** within the same ALS subtype

ARMOR

Primary Endpoint

- Safety and tolerability (up to Week 48)

Secondary Endpoints

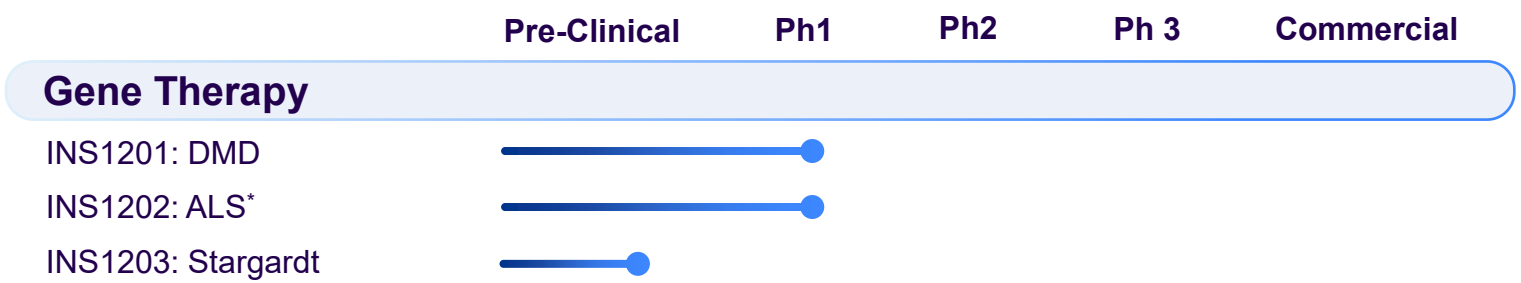
- Recommended Phase 2 dose (RP2D) (up to Week 48)

Exploratory Endpoints

- Viral vector shedding following the intrathecal administration of INS1202 by ddPCR

IDMC: Independent Data Monitoring Committee | ddPCR: droplet digital polymerase chain reaction | ALS: amyotrophic lateral sclerosis | SOD1: superoxide dismutase 1 gene

Neuro & Other Rare Therapeutic Area Pipeline



Anticipated Catalysts

’26/’27 | ASCEND DMD updates

’26/’27 | ARMOR ALS updates

2027 | IND for Stargardt filing

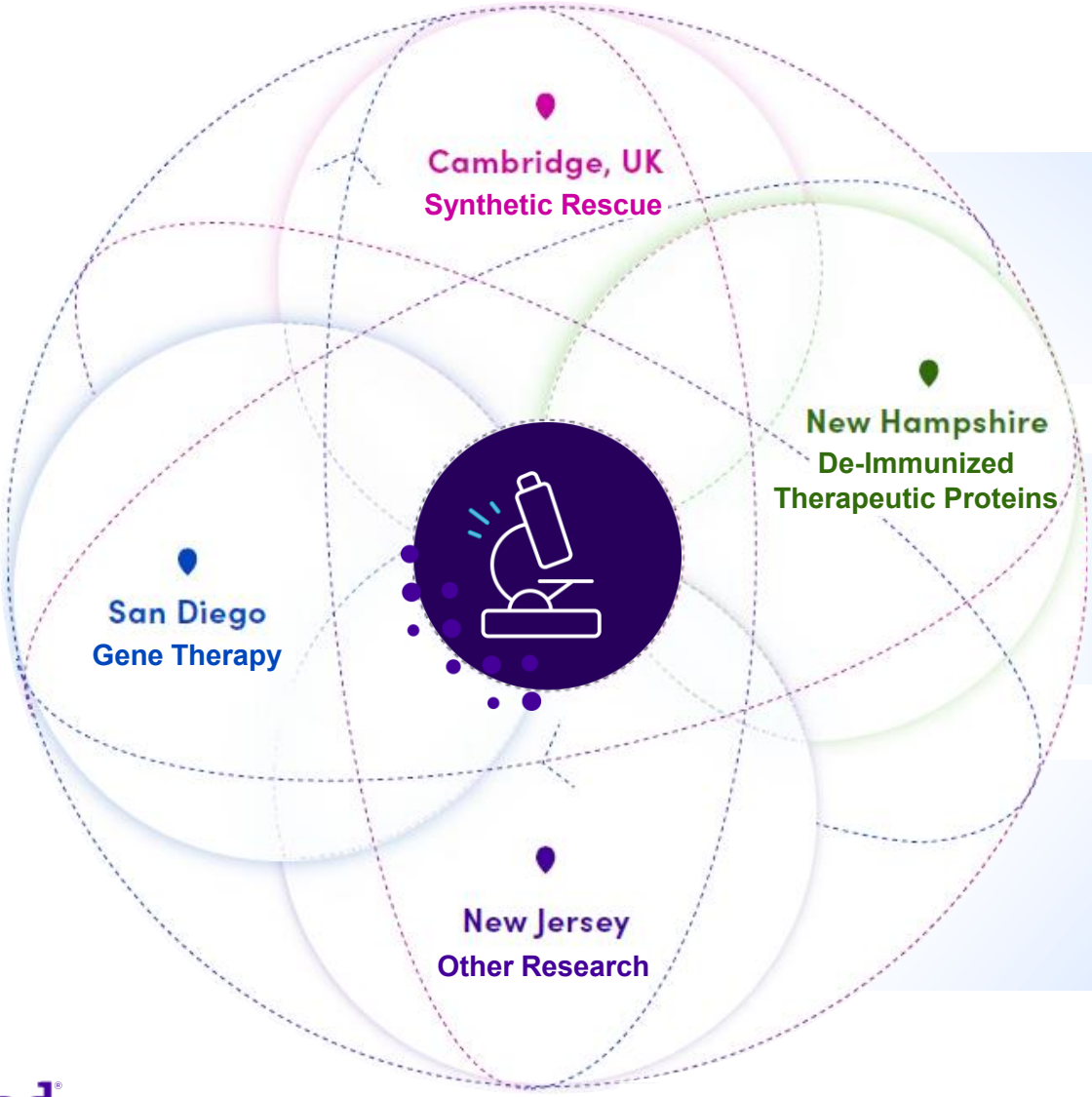
DMD: Duchenne muscular dystrophy | ALS: amyotrophic lateral sclerosis | IND: investigational new drug application | H: half | Ph: phase | * Studying both SOD1 (superoxide dismutase 1 gene) and sporadic ALS

Research Engine

PRE-CLINICAL PROGRAMS & BUSINESS DEVELOPMENT

insmed®

Multi-Dimensional Early-Stage Research Portfolio



Number of Active Pre-Clinical Programs >30

% of Overall Spend on Pre-Clinical Programs <20%

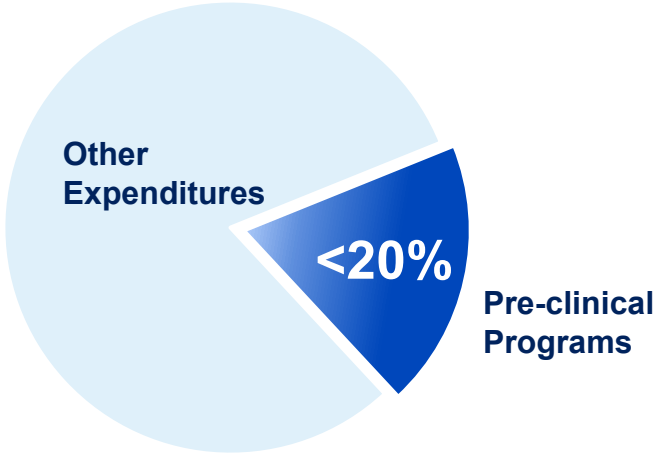
Estimated Number of INDs Filed Per Year 1-2

IND: investigational new drug application

Pre-Clinical Research Programs and Business Development Expected to Fuel Future Waves of Growth

Our Approach

Low upfront costs to acquire technologies



Low ongoing expense

Our Pre-Clinical Platforms

- Intrathecally Delivered Gene Therapy
- End-Joining Gene Therapy
- Deimmunized Protein Engineering Using AI
- Synthetic Rescue

IND: investigational new drug application | AI: artificial intelligence | RNA: ribonucleic acid

Our Culture Is Our Greatest Strength

In a recent survey*

>90% of employees

who responded said they felt:

Proud *to work at Insmed*

Inspired *by what we do*

Confident *in Insmed's future*

Driven *to do their best work*

Accolades that span the globe

Great Place To Work. Certified JUL 2026-JUL 2027 USA

Handshake EARLY TALENT AWARDS 2026 Winner

Science 2025 TOP EMPLOYER

2026 BEST PLACES to WORK BioSpace

THE SUNDAY TIMES Best Places to Work 2026 MEDIUM ORGANISATION

insmed

* The 2025 annual Insmed Pulse Survey included 92% participation across the organization

Appendix

Strong, Long-Dated Patent Exclusivity

	U.S.		Japan		EU	
	Current Exclusivity	Potential Exclusivity	Current Exclusivity	Potential Exclusivity	Current Exclusivity	Potential Exclusivity
ARIKAYCE	2035	2041[a]	2035	2041[a]	2035	2041[a]
BRINSUPRI	2040	2040+[b]	2039	2040+[c]	2035	2040[c]
TPIP	2034	2041[d]	2034	2041[d]	2034	2041[d]

U.S.: United States | [a] Based on U.S. Patent Application No.18/024,040 and ex-U.S. counterpart applications issuing as patents. Additionally, given the complexity of drug product (liposomal inhalation with specific nebulizer), required bioequivalence testing could be difficult and lead to few generic entrants.| [b] Based on potential patent term extension (PTE) in the U.S. and U.S. Application No. 16/975,292, which has been allowed, issuing in the U.S. | [c] Based on European SPC (supplementary protection certificate) and Japan PTE being capped at 5 years | [d] Based on U.S. Application No. 18/513,377 and ex-U.S. counterparts issuing as a patent

Manufacturing Country of Origin

ARIKAYCE

API

China[1]

Drug Product

RESILIENCE — Canada

ThermoFisher SCIENTIFIC — UK
To come online

Brensocatib

API

ESTEVE — Spain

Drug Product

ThermoFisher SCIENTIFIC — Canada

TPIP

API

CHIROGATE — Taiwan

Drug Product

Lonza — U.S.

Project underway to establish brensocatib **secondary source manufacturing** in the **U.S.**

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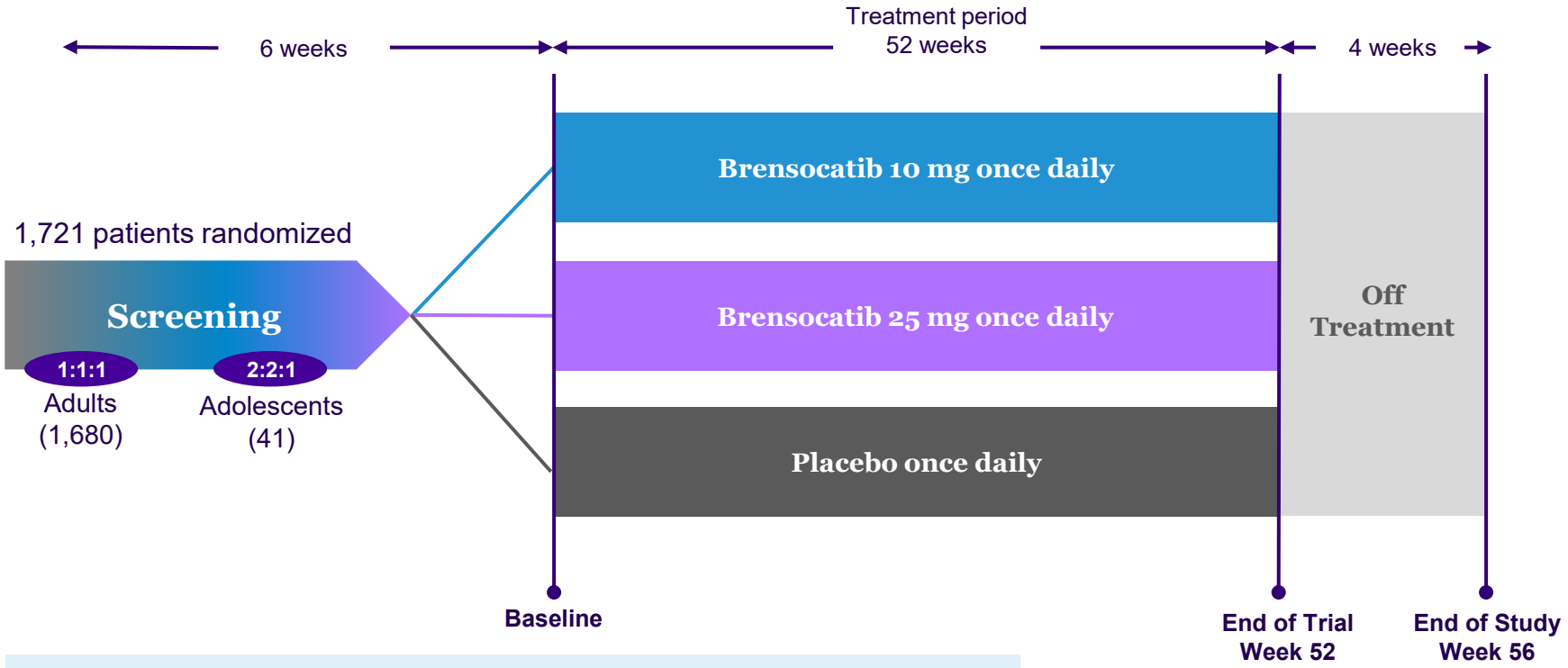
API: active pharmaceutical ingredient | U.S.: United States | UK: United Kingdom | [1] Amikacin sulfate starting materials are fermented and synthesized in China and the API is then finished at ACS Dobfar in Italy

Brensocatib Phase 3 in Bronchiectasis: Aspen

NCT04594369 Trial summary



Adults Stratification

- Sputum *Pseudomonas aeruginosa* culture status at screening (positive or negative)
- Number of exacerbations in the prior 12 months (2 or ≥3)
- Geographic region (Europe, Japan, North America, or ROW)

ASPEN

Primary Endpoint

- Annualized rate of adjudicated pulmonary exacerbations* over 52 weeks

Secondary Endpoints (Hierarchical)

- Time to first pulmonary exacerbation
- Proportion of patients who remained exacerbation-free
- Change from baseline in post-bronchodilator FEV_1 at week 52
- Annualized rate of severe exacerbations
- Change from baseline in QoL-B Respiratory Symptom Domain score at week 52

NCFB / Bronchiectasis: non-cystic fibrosis bronchiectasis | FEV_1: forced expiratory volume in 1 second (a key measure of lung function) | QoL-B: Quality of Life-Bronchiectasis Questionnaire | ROW: rest of world | * Defined as the presence of ≥3 of the following symptoms for at least 48 hours, resulting in a physician's decision to prescribe systemic antibiotics: (1) increased cough, (2) increased sputum production or change in sputum consistency, (3) increased sputum purulence, (4) increased breathlessness and/or decreased exercise tolerance, (5) fatigue and/or malaise, or (6) hemoptysis

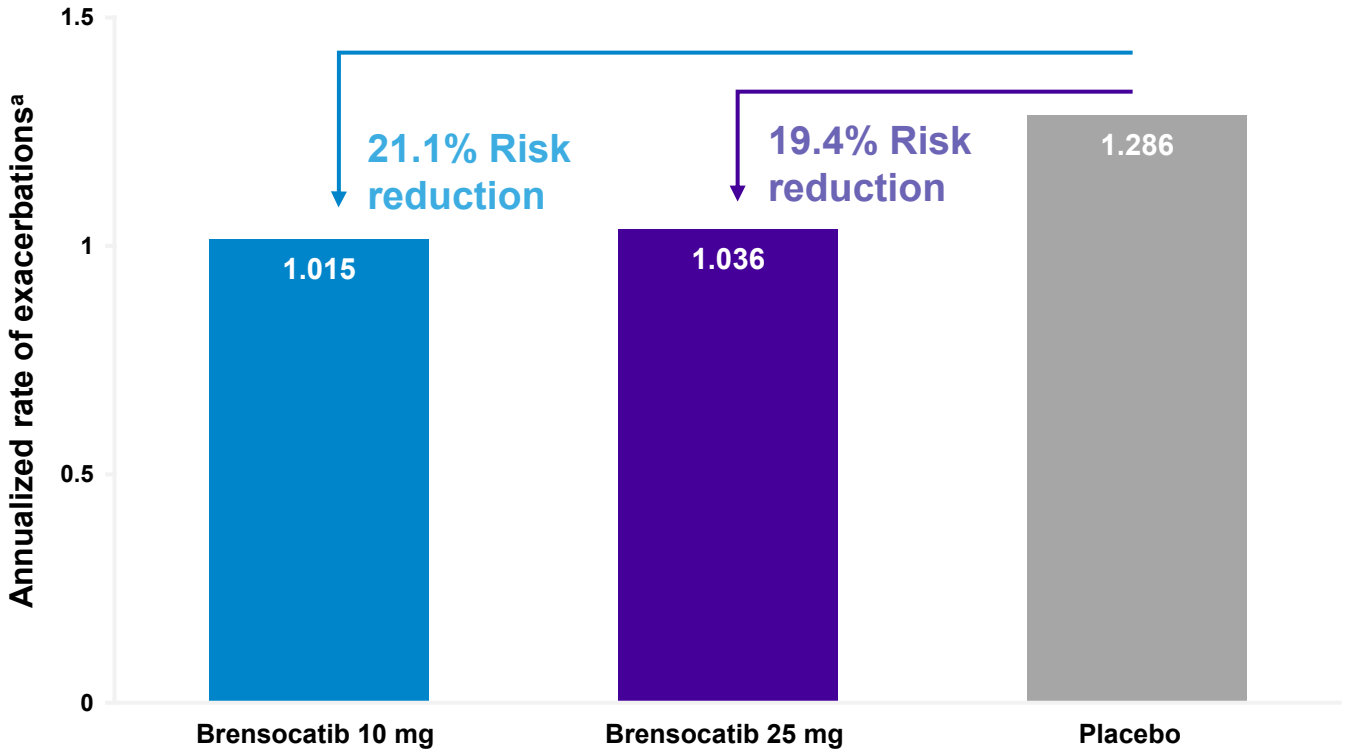
Phase 3 ASPEN Study a Clear Win: Primary Endpoint Achieved Statistical Significance on Both Doses

	Brensocatib 10 mg compared to placebo		Brensocatib 25 mg compared to placebo	
Primary Endpoint				
Reduction in annualized rate of PEs	21.1%	p = 0.0019*	19.4%	p = 0.0046*
Secondary Endpoints				
Prolongation of time to first PE	18.7%	p = 0.0100*	17.5%	p = 0.0182*
Increase in odds of remaining exacerbation free over 52 weeks	41.2%	p = 0.0059*	40.0%	p = 0.0074*
Change from baseline in post-bronchodilator FEV_1 at week 52	11 mL	p = 0.3841	38 mL	p = 0.0054*
Reduction in annualized rate of severe PEs	25.8%	p = 0.1277	26.0%	p = 0.1025
Change from baseline in the QoL-B Respiratory Score at week 52	2.0 points	p = 0.0594	3.8 points	p = 0.0004^

NCFB / Bronchiectasis: non-cystic fibrosis bronchiectasis | PE: pulmonary exacerbation | FEV_1: forced expiratory volume in 1 second (a key measure of lung function) | QoL-B: Quality of Life-Bronchiectasis Questionnaire | mg: milligram | * statistically significant | ^ nominally significant p-value

ASPEN: Annualized Rate of Adjudicated Pulmonary Exacerbations Over 52 Weeks

Primary endpoint



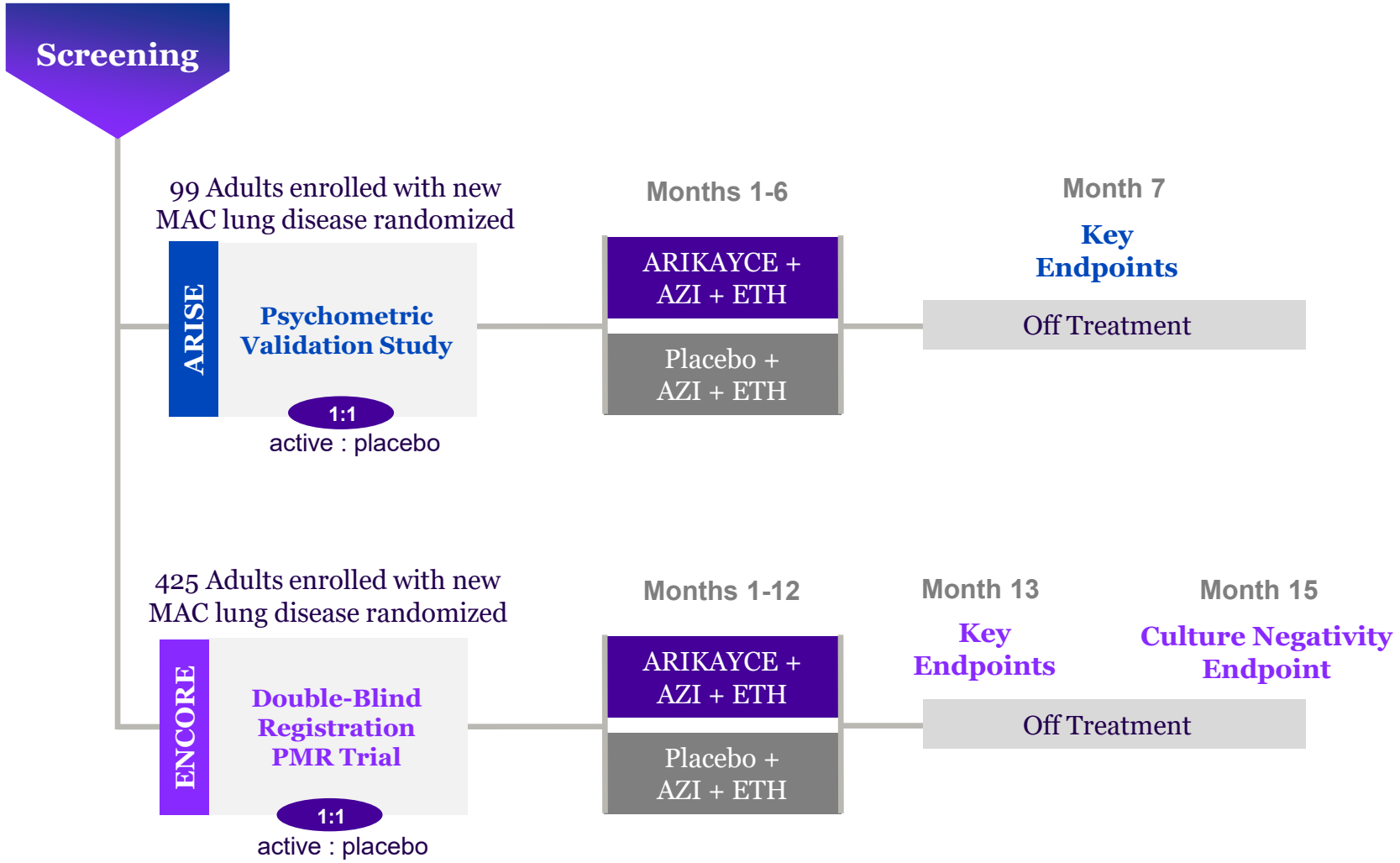
	Brensocatib 10 mg n=583	Brensocatib 25 mg n=575
Rate ratio vs. placebo (95% CI)	0.789 (0.680–0.916)	0.806 (0.694–0.936)
P-value	0.0019[b]	0.0046[b]

Risk Reduction Consistent Across Nearly All Pre-specified Subgroups

ITT: intention-to-treat | NCFB / Bronchiectasis: non-cystic fibrosis bronchiectasis | mg: milligram | n: number of patients | [a] Exacerbations were adjudicated events in the ITT analysis set analyzed using a negative binomial model | [b] *P* value is statistically significant when adjusted for multiplicity control

ARIKAYCE Phase 3 Programs to Potentially Expand MAC Indication

NCT04677543 & NCT04677569 Trial summaries



ARISE

Primary Endpoint

- Demonstrate reliability, validity and responsiveness of the patient reported outcome (PRO) / symptom scores (at Baseline / Baseline to Month 7)

Select Secondary Endpoints

- Demonstrate effect of ARIKAYCE on culture conversion / time to first culture conversion (Month 7)
- Recurrence of MAC relapse or new infection (Month 7)

ENCORE

Primary Endpoint

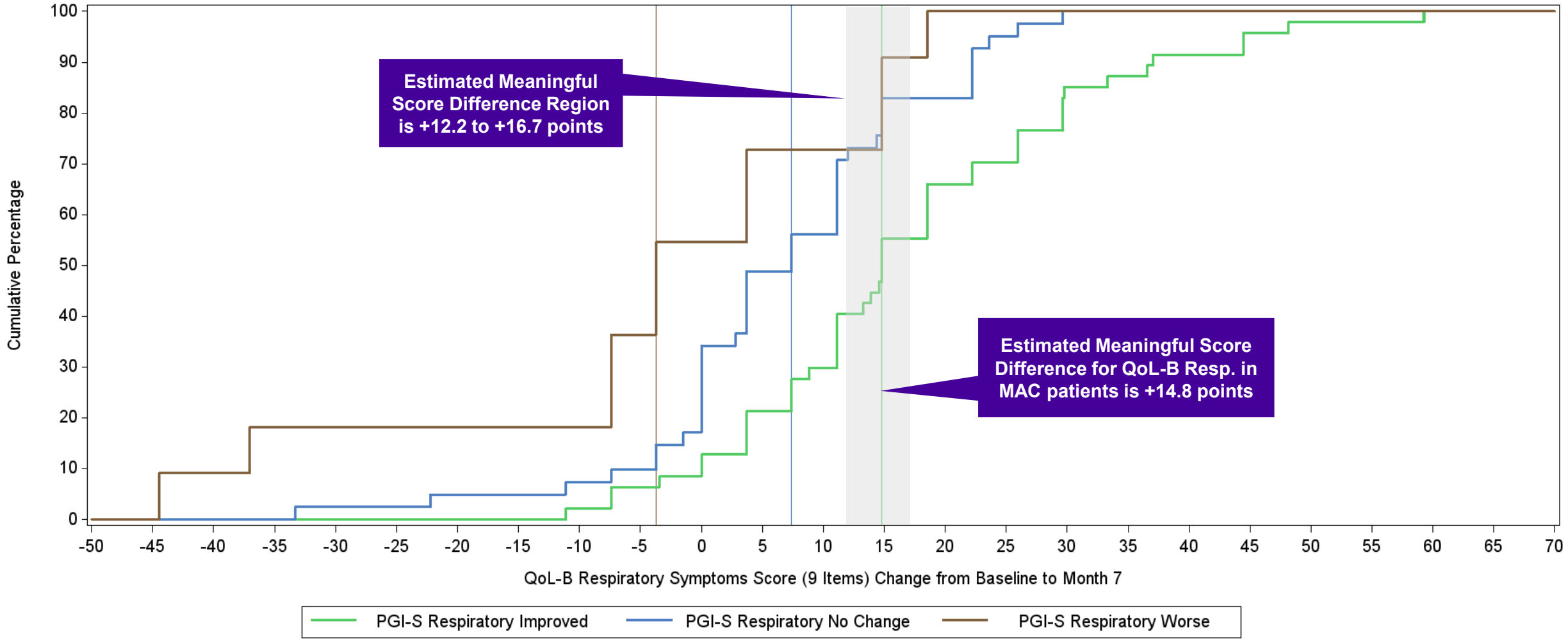
- Change from **baseline respiratory symptom score** at Month 13 (one month off treatment)

Select Secondary Endpoints

- Proportion of patients achieving culture conversion at Months 6, 12, and 13
- Proportion of patients achieving **durable culture conversion** at Month 15 (three months off treatment)

MAC / MACLD: *Mycobacterium avium complex* lung disease | AZI: Azithromycin | ETH: Ethambutol | PMR: post marketing requirement

ARISE: QoL-B Respiratory Score Changes* Show Clear Separation When PGI-S Category Improved vs. No Change or Decline



QoL-B: Quality of Life-Bronchiectasis Respiratory Domain questionnaire | PGI-S: Patient Global Impression of Severity | MAC: *Mycobacterium avium* complex | * Includes patient data from both the treatment and control arm of the ARISE study

ARISE: Comparison Between Treatment Arms Shows Clear Favorable Trend for ARIKAYCE Arm

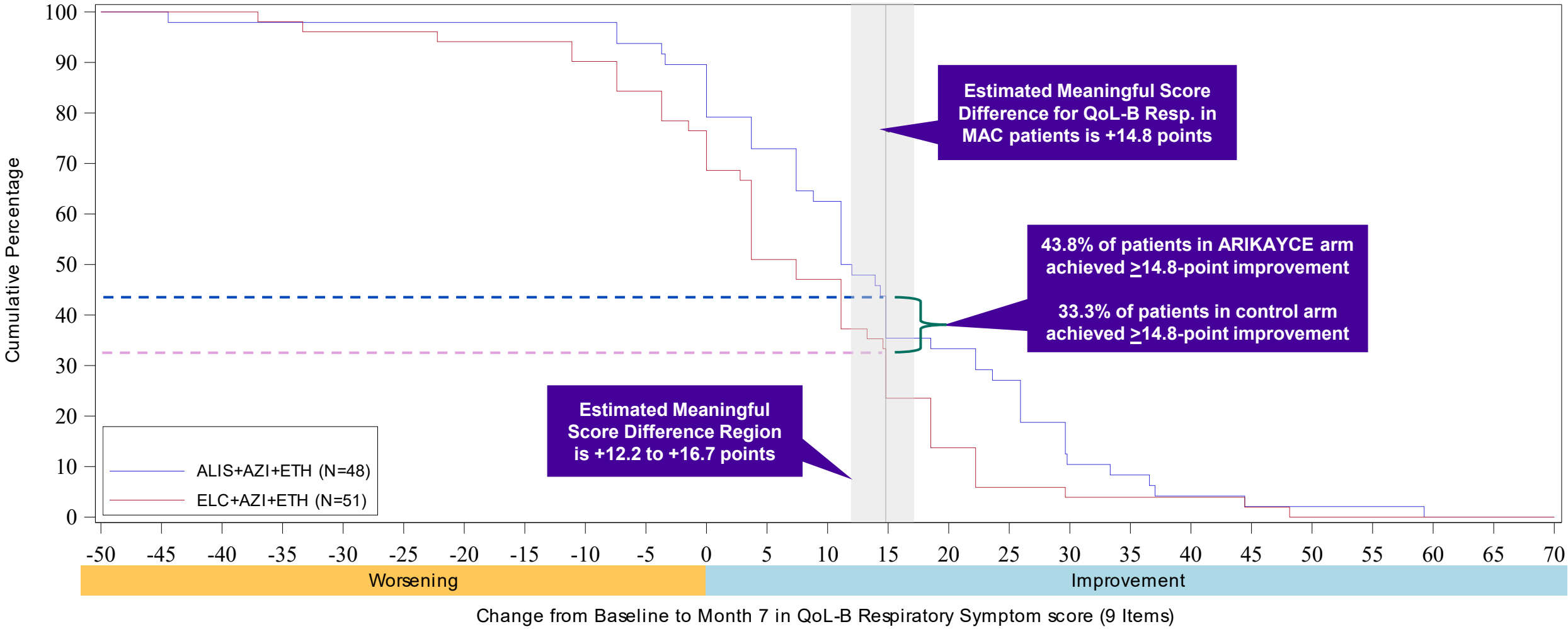
	QoL-B Respiratory Domain		
	ALIS+AZI+ETH N=48	ELC+AZI+ETH N=51	Difference
# of Participants Evaluated for Change from Baseline to Month 7	43	48	
# of Missing Change from Baseline to Month 7 Value	5	3	
Change in PRO Score from Baseline to Month 7 (LS-Mean)	12.24	7.76	4.48
(95% Confidence Interval)	(7.96, 16.53)	(3.76, 11.77)	(-0.97, 9.93)
p-value			0.1073

ITT analysis with multiple imputation for missing data

ANCOVA model includes change from baseline as response variable and treatment, baseline Resp Score, and history of MAC lung infection as independent variables.

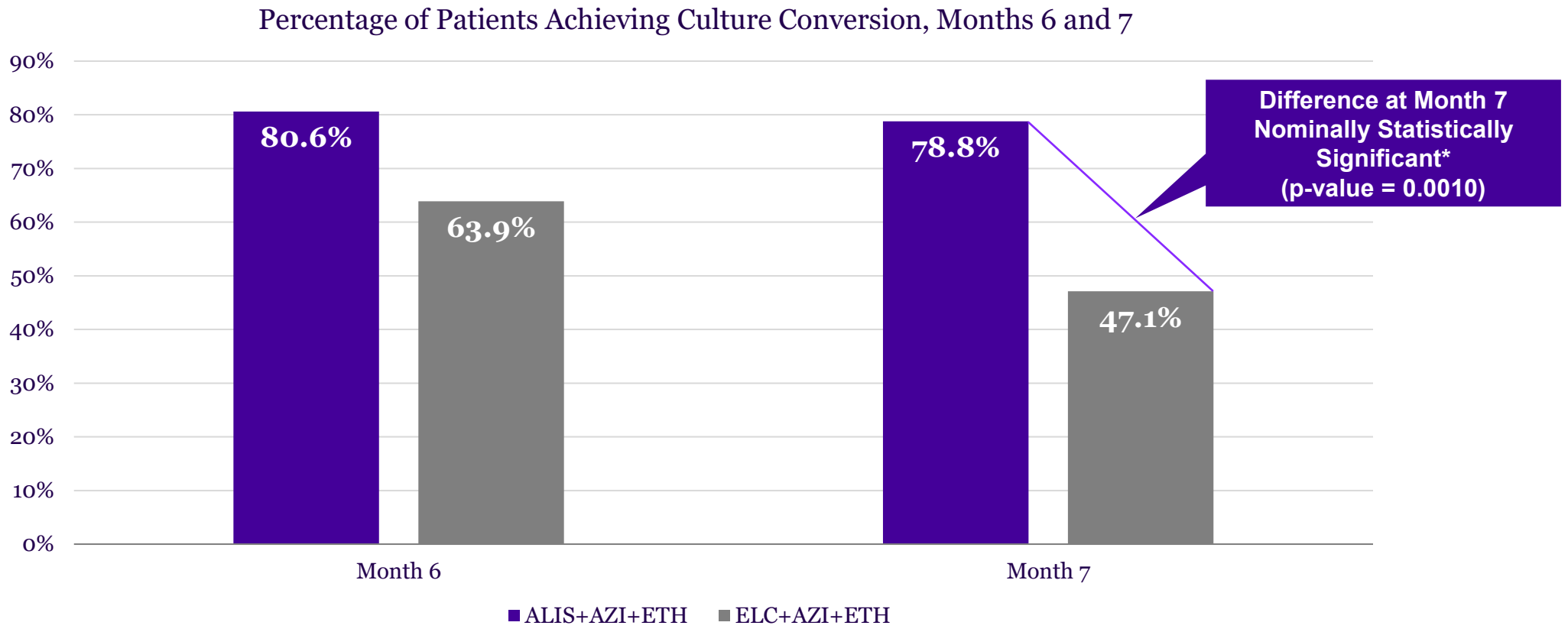
MAC / MACLD: *Mycobacterium avium* complex lung disease | ALIS: amikacin liposome inhalation suspension | AZI: azithromycin | ELC: empty liposome control | ETH: ethambutol | LS: least-squares | QoL-B: Quality of Life-Bronchiectasis Respiratory Domain questionnaire | PRO: patient-reported outcome | MAC: *Mycobacterium avium* complex | ITT: intention-to-treat | N: number of patients

ARISE: QoL-B Respiratory Score Changes from Baseline to Month 7 Show Clear Separation for ARIKAYCE Group



CDF: cumulative distribution function | ALIS: amikacin liposome inhalation suspension | AZI: azithromycin | ELC: empty liposome control | ETH: ethambutol | QoL-B: Quality of Life-Bronchiectasis Respiratory Domain questionnaire | MAC / MACLD: *Mycobacterium avium* complex lung disease | N/n: number of patients

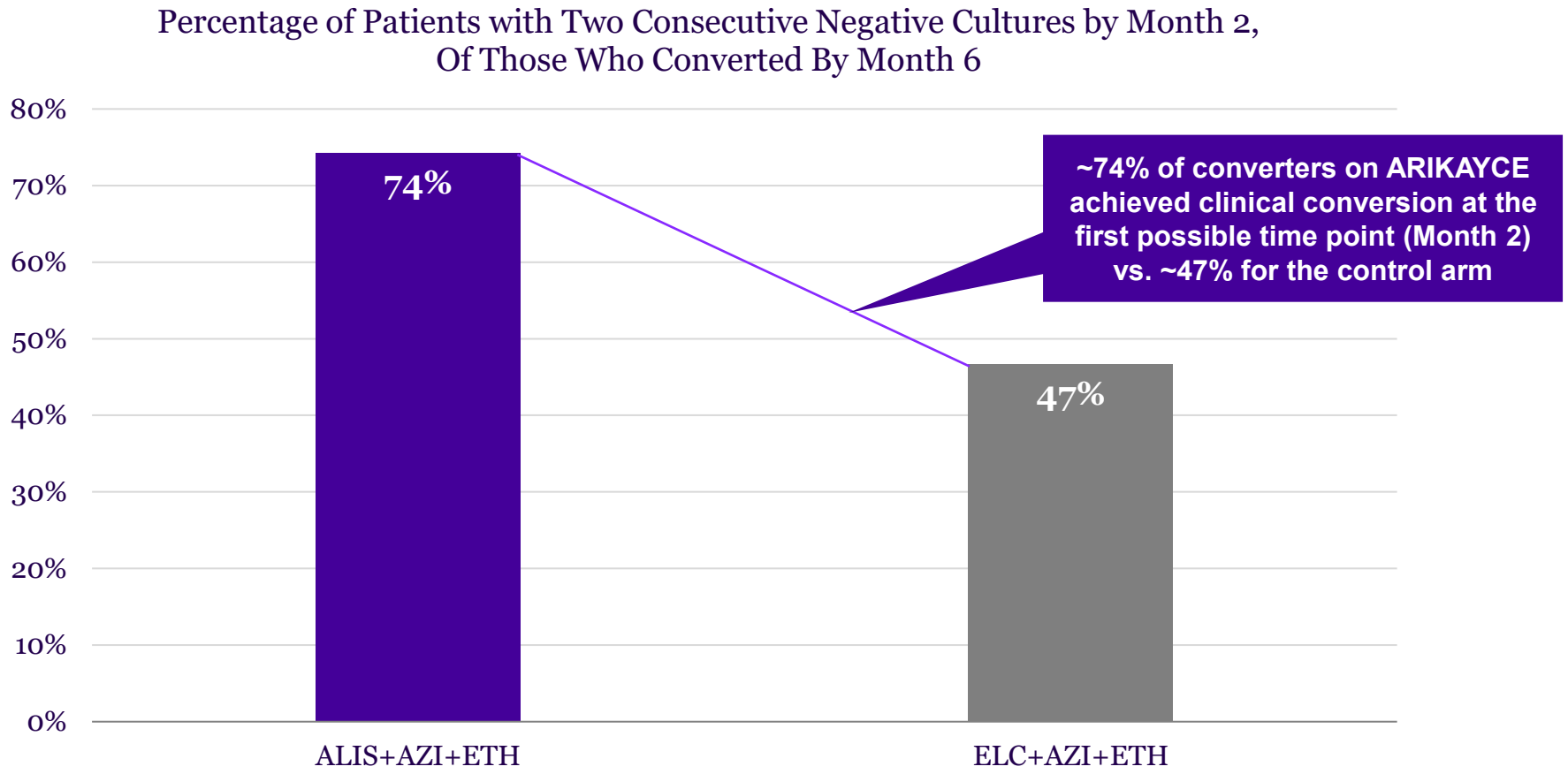
ARISE: Significantly* Higher, More Persistent Culture Conversion in ARIKAYCE Arm



Proportions estimated by Standardized Logistic Regression with treatment group and History of MAC Lung Infection as factors in the model with multiple imputation for missing data.

ALIS: amikacin liposome inhalation suspension | AZI: azithromycin | ELC: empty liposome control | ETH: ethambutol | MAC / MACLD: *Mycobacterium avium* complex lung disease | * "Nominally statistically significant" because no hierarchical testing or adjustment for multiplicity was conducted in ARISE

ARISE: For Those Who Achieved Culture Conversion, Patients in ARIKAYCE Arm Converted Faster



ALIS: amikacin liposome inhalation suspension | AZI: azithromycin | ELC: empty liposome control | ETH: ethambutol | MAC: *Mycobacterium avium* complex

ARISE: Correlation Shown Between Culture Conversion and QoL-B Respiratory Score Changes in ARIKAYCE Arm

	ALIS+AZI+ETH (N=48)		
	Culture Converted by Month 6	Not Culture Converted by Month 6	Difference
Change in QoL-B Resp. Score (Baseline to Month 7)	+15.74	+3.53	**+12.21**
(95% Confidence Interval)	(+11.45, +20.03)	(-5.34, +12.41)	(+2.33, +22.08)
p-value			**0.0167**
	Culture Converted by Month 7	Not Culture Converted by Month 7	Difference
Change in QoL-B Resp. Score (Baseline to Month 7)	+14.89	+4.50	**+10.39**
(95% Confidence Interval)	(+10.47, +19.31)	(-4.40, +13.40)	(+0.42, +20.37)
p-value			**0.0416**

ANCOVA model includes change from baseline as the response variable and baseline Resp Score, and culture conversion status as independent variables using observed data.

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ALIS: amikacin liposome inhalation suspension | AZI: azithromycin | ETH: ethambutol | LS: least-squares | QoL-B: Quality of Life-Bronchiectasis Respiratory Domain questionnaire | MAC: *Mycobacterium avium* complex

ARISE: No New or Unexpected Safety Signals in ARISE

All serious TEAEs unrelated to ARIKAYCE

	ALIS+AZI+ETH N=48	ELC+AZI+ETH N=51	Total N=99
Study completion (%)	44 (91.7)	48 (94.1)	92 (92.9)
Treatment completion with all 3 drugs (%)	35 (72.9)	47 (92.2)	82 (82.8)
Early ALIS/ELC discontinuation (%)	11 (22.9)	4 (7.8)	15 (15.2)
Any TEAE (%)	44 (91.7)	41 (80.4)	85 (85.9)
Dysphonia (%)	20 (41.7)	2 (3.9)	22 (22.2)
Cough (%)	13 (27.1)	4 (7.8)	17 (17.2)
Diarrhea (%)	13 (27.1)	13 (25.5)	26 (26.3)
COVID-19 (%)	6 (12.5)	5 (9.8)	11 (11.1)
# Participants with Serious TEAE (%)	7 (14.6)	3 (5.9)	10 (10.1)

ALIS: amikacin liposome inhalation suspension | AZI: azithromycin | ELC: empty liposome control | ETH: ethambutol | TEAE: treatment-emergent adverse event | MAC: *Mycobacterium avium* complex | N: number of patients

Baseline Characteristics Were Well-Balanced Across Arms

ENCORE

	ARIKAYCE Arm[1] N=213	Comparator Arm[2] N=212	Total N=425
Age: Median at Screening, Years	68.0	69.0	68.0
≥65, % (n)	67.1% (143)	70.3% (149)	68.7% (292)
Sex: Female, % (n)	80.3% (171)	78.3% (166)	79.3% (337)
Geographic Region: % (n)*			
North America	24.4% (52)	25.5% (54)	24.9% (106)
Japan	20.2% (43)	19.3% (41)	19.8% (84)
Europe	26.8% (57)	25.9% (55)	26.4% (112)
Rest of the World	28.6% (61)	29.2% (62)	28.9% (123)
Race: % (n)			
White	62.9% (134)	62.7% (133)	62.8% (267)
Asian	32.4% (69)	35.4% (75)	33.9% (144)
Other	4.7% (10)	1.9% (4)	3.3% (14)
History of MAC Lung Infection[3]: Initial,% (n)*	82.2% (175)	82.5% (175)	82.4% (350)
Mean Baseline† Respiratory Symptom Score[4] (RSS), Points	63.91	61.52	62.72
Mean Baseline PROMIS Fatigue T-Score, Points	55.23	54.88	55.05

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MAC / MACLD: *Mycobacterium avium* complex lung disease | AZI: Azithromycin | ETH: Ethambutol | N/n: number of patients | [1] ARIKAYCE (590 mg) + macrolide-based background regimen consisting of AZI (250 mg) and ETH (15 mg/kg) | [2] Empty liposome control placebo + macrolide-based background regimen consisting of AZI and ETH | [3] Initial diagnosis defined as a patient being diagnosed with MAC lung infection for the first time. Subsequent diagnosis defined as a previously infected MAC patient being reinfected with the disease (new infection). A reinfected patient is not the same as a refractory patient, who did not culture convert on initial therapy and must add or switch therapies to treat the same infection | [4] RSS ranges from 0 to 100, with positive change indicating improvement | † Baseline value is the last non-missing value prior to the first dose of ARIKAYCE or empty liposomal control placebo | * randomization stratification factors

RSS: Statistically Significant Improvement in RSS[1] Observed With ARIKAYCE at **Month 13**

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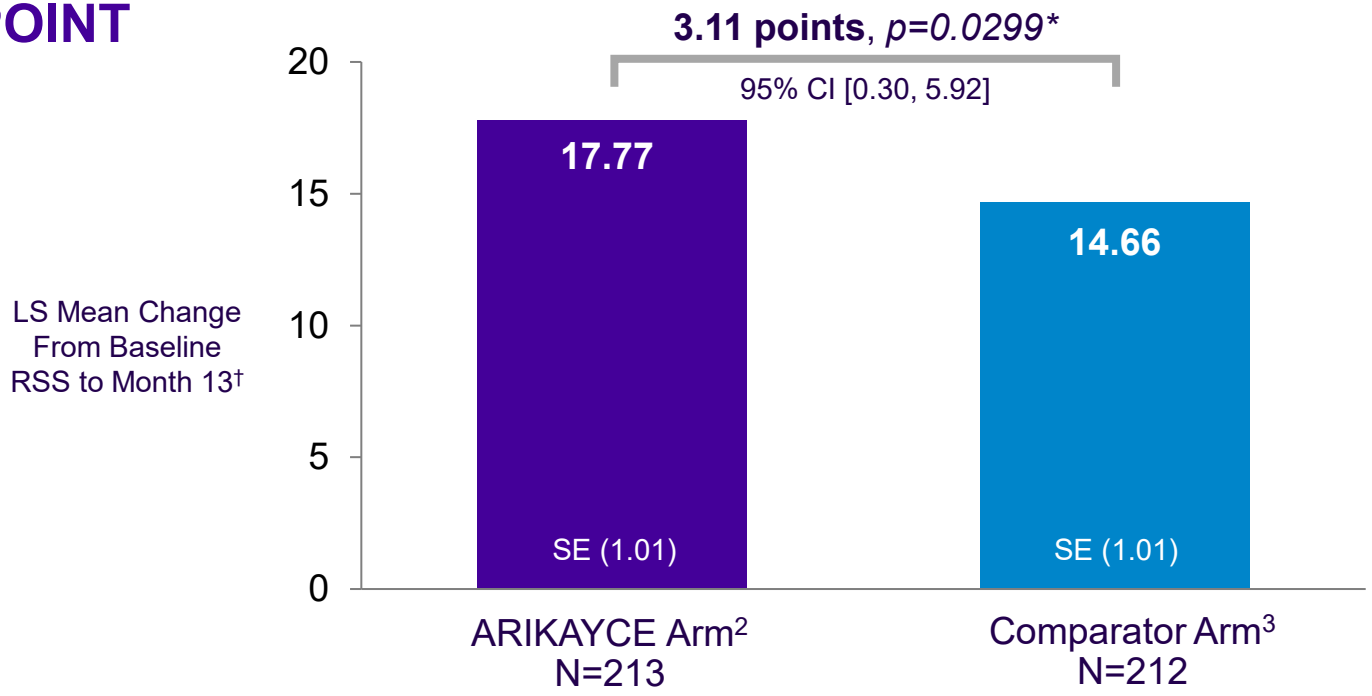
PRIMARY ENDPOINT



Change From Baseline RSS to Month 15

Symptom benefit at Month 15 expands to a **4.80-point difference**[4,†], favoring the **ARIKAYCE arm** *(p=0.0015^)*

Exploratory Endpoint

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MAC / MACLD: *Mycobacterium avium* complex lung disease | AZI: Azithromycin | ETH: Ethambutol | RSS: Respiratory Symptom Score | LS: least-squares | SE: standard error | CI: confidence interval | SAP: statistical analysis plan | N: number of patients | [1] RSS ranges from 0 to 100, with positive change indicating improvement | [2] ARIKAYCE (590 mg) + macrolide-based background regimen consisting of AZI (250 mg) and ETH (15 mg/kg) | [3] Empty liposome control placebo + macrolide-based background regimen consisting of AZI and ETH | [4] LS mean changes from baseline RSS to Month 15 for the ARIKAYCE and Comparator arms were 16.63 points and 11.83 points, respectively | † ANCOVA (analysis of covariance) model includes change from baseline as the dependent variable and treatment, baseline RSS, history of MAC lung infection (initial or subsequent), and region as independent variables. Multiple imputations are applied to impute the missing RSS scores in the analysis using ANCOVA according to the type of incurrent events and the assumptions of mission data mechanism described in the SAP | * statistically significant | ^ nominal not adjusted for multiplicity control

Responder Analysis: ARIKAYCE Arm Showed Higher Rates of Clinically Meaningful Improvement in RSS[1] at **Month 13**

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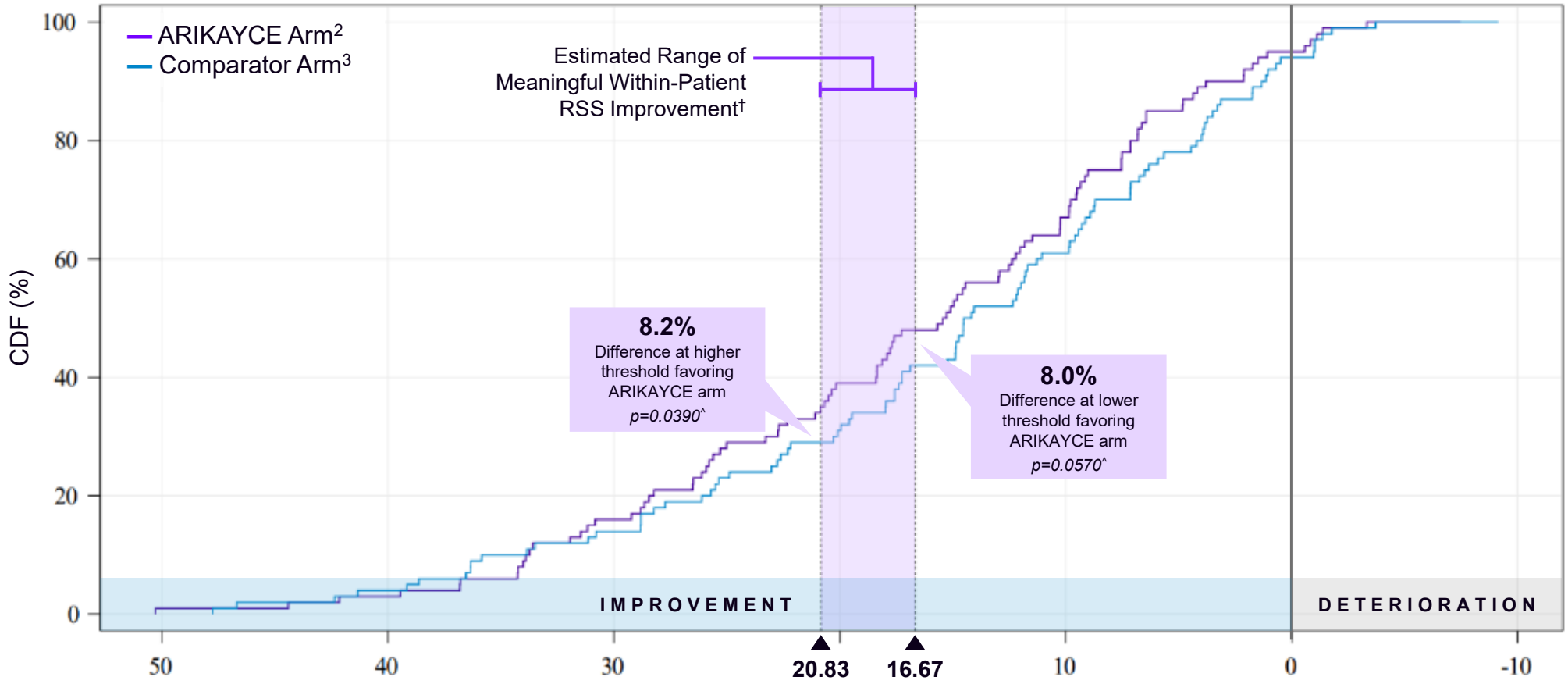


Meaningful Within-Patient Change in RSS

Separation observed between arms **consistently favored ARIKAYCE** across a range of possible RSS improvement thresholds that could be determined clinically meaningful by the FDA

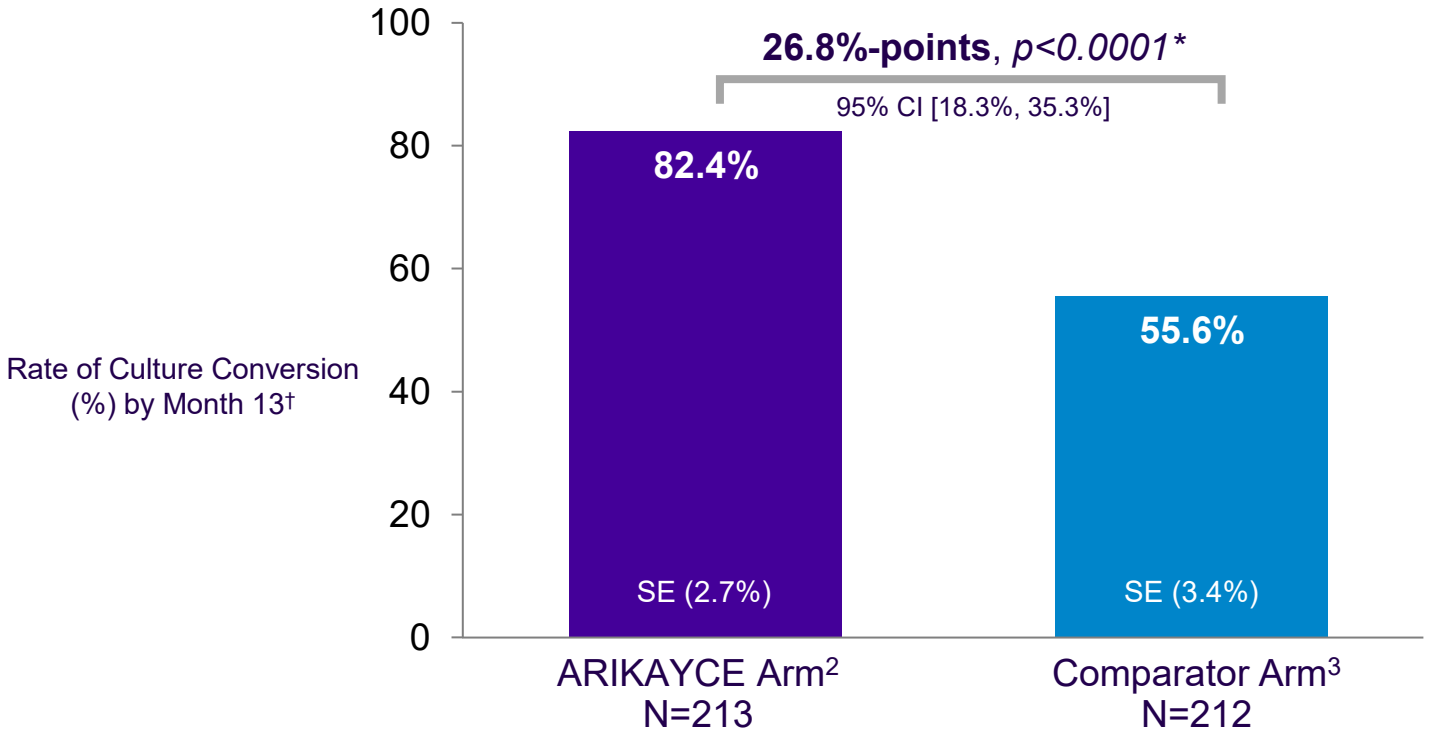
Secondary Endpoint

MAC / MACLD: *Mycobacterium avium* complex lung disease | AZI: Azithromycin | ETH: Ethambutol | RSS: Respiratory Symptom Score | CDF: covariate-adjusted cumulative distribution function | FDA: Food and Drug Administration | MWPC: meaningful within-patient change | [1] RSS ranges from 0 to 100, with positive change indicating improvement | [2] ARIKAYCE (590 mg) + macrolide-based background regimen consisting of AZI (250 mg) and ETH (15 mg/kg) | [3] Empty liposome control placebo + macrolide-based background regimen consisting of AZI and ETH | Note: 53.4% of ARIKAYCE arm participants achieved the 16.67 MWPC in RSS threshold (vs. 45.4% in the Comparator arm) and 43.5% of ARIKAYCE arm participants achieved the 20.83 MWPC in RSS threshold (vs. 35.5% in the Comparator arm); using the standardized logistic regression (SLR); analysis includes treatment group, baseline, region, and history of MAC lung infection (initial or subsequent) as factors in model | ^ nominal not adjusted for multiplicity control | † Estimated threshold range established using data (prior to unblinding) from the Phase 3 ARISE and ENCORE studies

Culture Conversion: Statistically Significant Greater Proportion of ARIKAYCE Patients Achieved Culture Conversion[1] by **Month 13**

ENCORE

SECONDARY ENDPOINT



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MAC / MACLD: *Mycobacterium avium* complex lung disease | AZI: Azithromycin | ETH: Ethambutol | SAP: statistical analysis plan | SE: standard error | N: number of patients | [1] Conversion by Month 13 was defined as negative MAC cultures at Month 12 and Month 13 after applying adjustment rules as specified in the SAP | [2] ARIKAYCE (590 mg) + macrolide-based background regimen consisting of AZI (250 mg) and ETH (15 mg/kg) | [3] Empty liposome control placebo + macrolide-based background regimen consisting of AZI and ETH | † standardized logistic regression (SLR); analysis includes treatment group, region, and history of MAC lung infection (initial or subsequent) as factors in model. Multiple imputations are applied to impute the missing culture conversion results in the analysis using SLR model according to the type of incurrent events and the assumptions of missing data mechanism as described in the SAP | * statistically significant

Statistically Significant Greater Proportion of ARIKAYCE Patients Achieved **Durable Culture Conversion[1]** by **Month 15**

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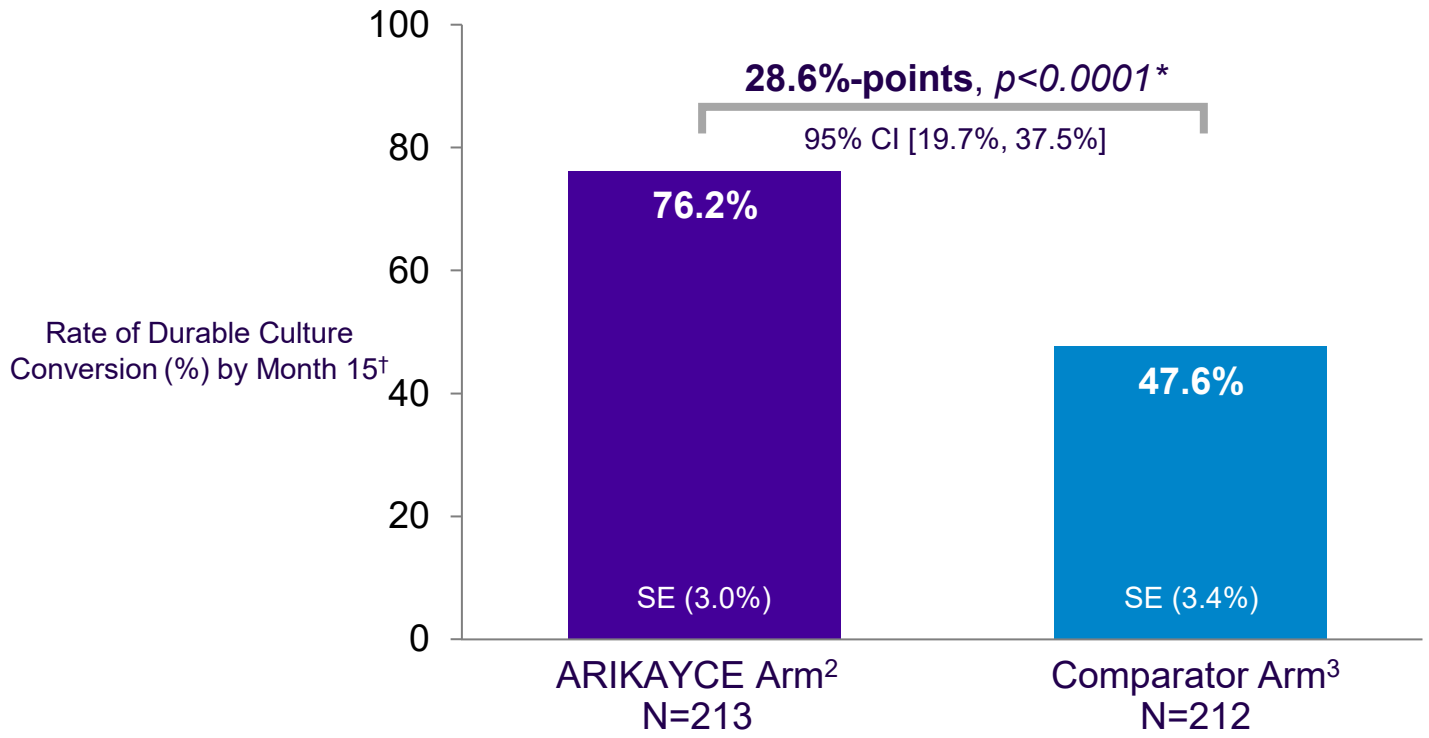
KEY SECONDARY ENDPOINT



MAC / MACLD: *Mycobacterium avium* complex lung disease | AZI: Azithromycin | ETH: Ethambutol | SAP: statistical analysis plan | SE: standard error | N: number of patients | [1] Durable converters at Month 15 are participants who achieved and maintained negative MAC cultures by Months 11, 12, 13 and 15 after applying adjustment rules as specified in the SAP | [2] ARIKAYCE (590 mg) + macrolide-based background regimen consisting of AZI (250 mg) and ETH (15 mg/kg) | [3] Empty liposome control placebo + macrolide-based background regimen consisting of AZI and ETH | † standardized logistic regression (SLR); analysis includes treatment group, region, and history of MAC lung infection (initial or subsequent) as factors in model. Multiple imputations are applied to impute the missing culture conversion results in the analysis using SLR model according to the type of incurrent events and the assumptions of missing data mechanism as described in the SAP | * statistically significant

Earlier and **Greater Culture Conversion**[1] Rates Were Achieved in ARIKAYCE Arm at Every Measured Timepoint

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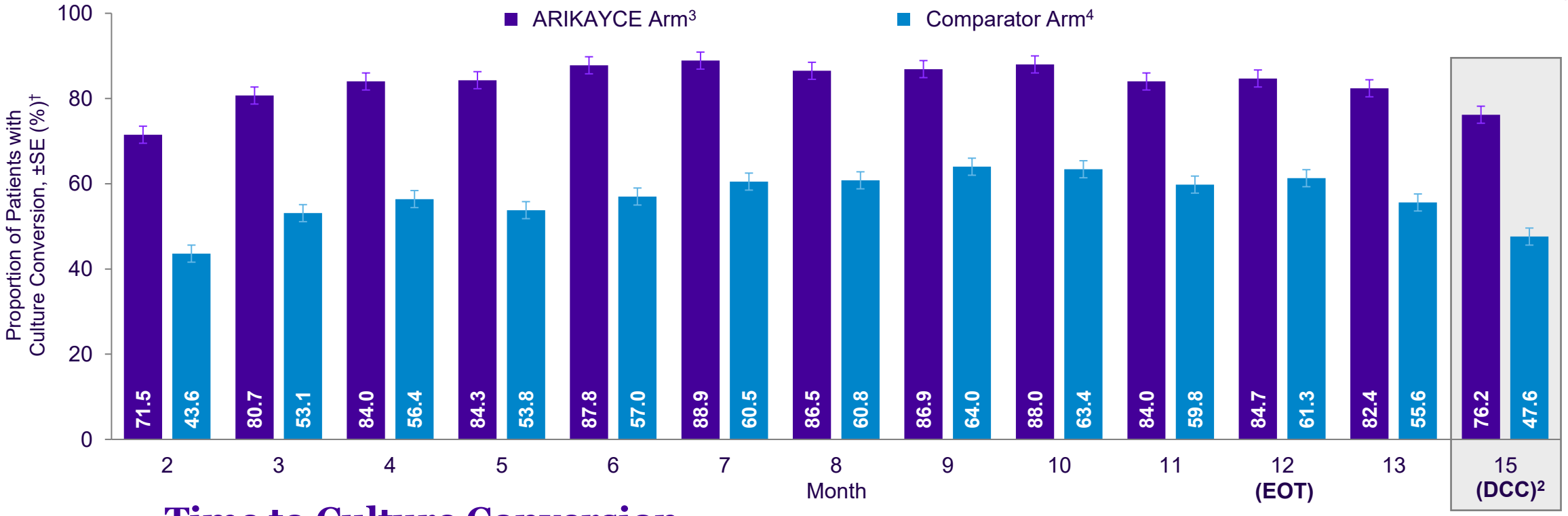

Time to Culture Conversion

ARIKAYCE patients were roughly twice as likely to achieve earlier culture conversion vs. active comparator patients‡

Exploratory Endpoint

MAC / MACLD: *Mycobacterium avium* complex lung disease | AZI: Azithromycin | ETH: Ethambutol | SE: standard error | SAP: statistical analysis plan | EOT: end of treatment | DCC: durable culture conversion | [1]Culture conversion rate at each visit from Month 2 to Month 13 is displayed as the second month of 2 consecutive negative cultures after applying adjustment rules as specified in the SAP | [2] Durable converters at Month 15 are participants who achieved and maintained negative MAC cultures by Months 11, 12, 13 and 15 after applying adjustment rules as specified in the SAP | [3] ARIKAYCE (590 mg) + macrolide-based background regimen consisting of AZI (250 mg) and ETH (15 mg/kg) | [4] Empty liposome control placebo + macrolide-based background regimen consisting of AZI and ETH | † standardized logistic regression (SLR); analysis includes treatment group, region, and history of MAC lung infection (initial or subsequent) as factors in model. Multiple imputations are applied to impute the missing culture conversion results in the analysis using SLR model according to the type of incurrent events and the assumptions of missing data mechanism as described in the SAP | ‡ ARIKAYCE arm achieved median time to culture conversion at Month 2 vs. Month 3 for the active comparator arm (Hazard Ratio of 2.03, suggesting that patients treated with ARIKAYCE were roughly twice as likely to achieve culture conversion (nominal p<0.0001, not adjusted for multiplicity control)

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Safety: No New or Unexpected Safety Signals Observed

	ARIKAYCE Arm[1] N=213		Comparator Arm[2] N=212	
DISPOSITION	**%**	**n**	**%**	**n**
Study Completion**	90.6%	193	93.4%	198
ARIKAYCE/Comparator Treatment Completion	81.7%	174	88.2%	187
ARIKAYCE/Comparator Discontinuation	18.3%	39	11.8%	25
SAFETY				
TEAES	98.1%	209	97.2%	206
Serious	14.1%	30	11.3%	24
Severe	15.0%	32	10.4%	22
Leading to ARIKAYCE/Comparator Discontinuation	14.6%	31	8.5%	18
Leading to Death	0.5%	1	0.5%	1
Most Common TEAEs Reported*				
Dysphonia	58.7%	125	8.5%	18
Cough	32.9%	70	14.6%	31
Fatigue	17.4%	37	11.3%	24
Dyspnea	16.4%	35	5.7%	12
Nausea	15.5%	33	12.7%	27
Headache	12.7%	27	11.8%	25

Tolerability profile of ARIKAYCE + multidrug therapy was **consistent with known profiles** of these therapies

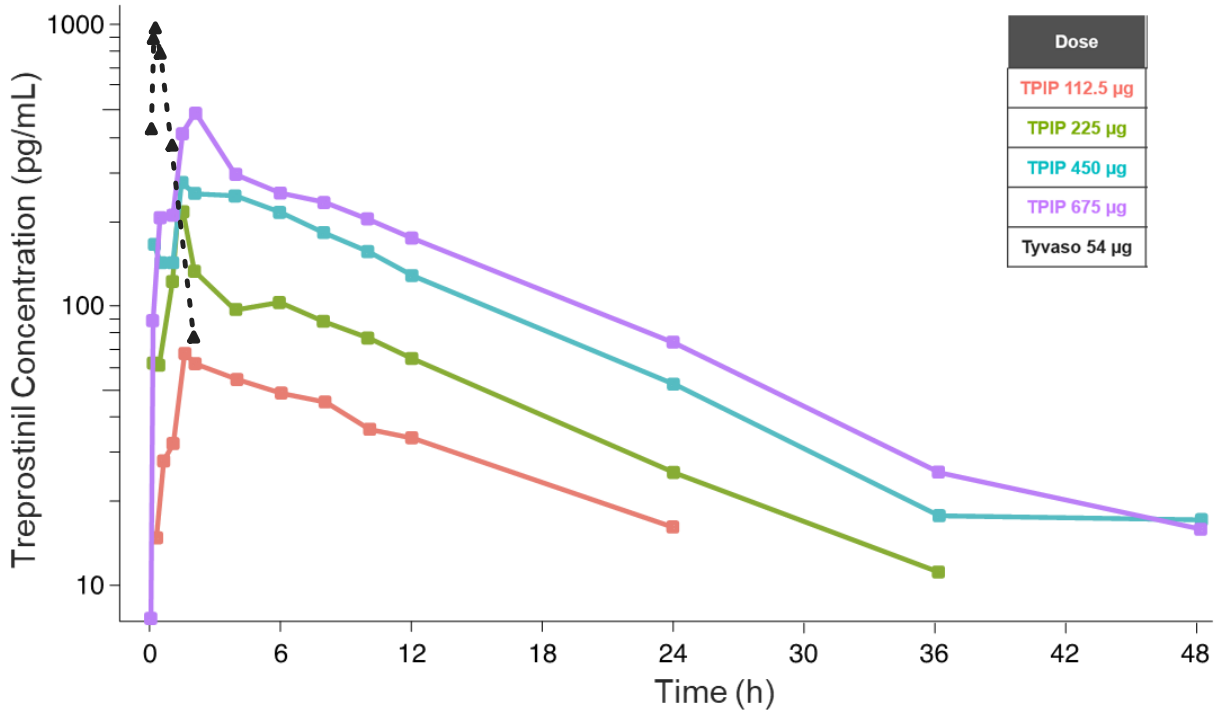
>90% completion observed for both study arms**

No deaths were considered ARIKAYCE- or placebo-related

MAC / MACLD: *Mycobacterium avium* complex lung disease | AZI: Azithromycin | ETH: Ethambutol | [1] ARIKAYCE (590 mg) + macrolide-based background regimen consisting of AZI (250 mg) and ETH (15 mg/kg) | [2] Empty liposome control placebo + macrolide-based background regimen consisting of AZI and ETH | N/n: number of patients | TEAE: treatment-emergent adverse event | * TEAEs that occurred in ≥10% of the ARIKAYCE arm and were elevated compared to the Comparator arm | ** Patients may discontinue one or more of the treatments in the study, but not discontinue the entire study

TPIP Phase 1 Study: Key Takeaways

- Safety profile was generally **well tolerated,** AEs were mild and **consistent with inhaled prostanoid**
- Tolerability was improved with **an up-titration approach**
- Findings suggest TPIP may be safely **dosed at nominal doses far in excess of TYVASO®**
- PK supports development of TPIP with **once daily dosing**
- TPIP showed substantially **lower C_{max} and longer half-life** than that of TYVASO®
- Future studies would use an up-titration dosing schedule to the maximum individual tolerated dose **exceeding 600 µg once daily**



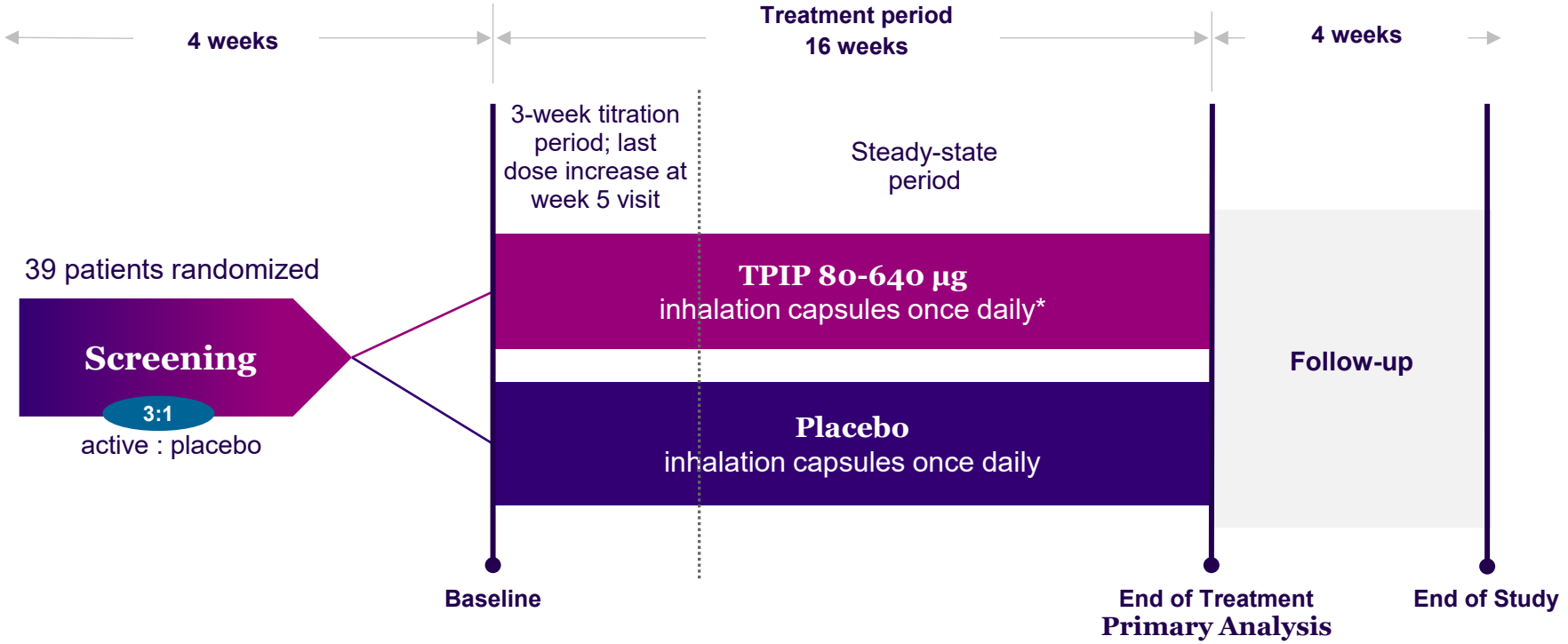
Supports the potential for improved tolerability, efficacy and convenience

TPIP showed substantially lower Cmax and longer half-life

TPIP: treprostinil palmitil inhalation powder | AE: adverse event | C_{max}: highest concentration of a drug in blood, fluid, or target organ after dosing | PK: pharmacokinetics

TPIP Phase 2a in PH-ILD

NCT05176951 Trial summary



PH-ILD Trial

Primary Endpoints

- Safety and tolerability
- Oxygenation at exercise

Secondary Endpoints

- Pharmacokinetics

Exploratory Endpoints

- Improvement in 6-Minute Walk Distance (6MWD)
- Improvement in biomarkers of cardiac stress (NT-proBNP)
- Improvement in lung function and pulmonary vascular volume (FRI)
- Improvements in Quality of Life (CAMPHOR questionnaire)
- Clinical worsening*

TPIP: treprostinil palmitil inhalation powder | PH-ILD: pulmonary hypertension due to interstitial lung disease | 6MWD: 6-minute walk distance | NT-proBNP: N-terminal pro-B-type natriuretic peptide | FRI: functional respiratory imaging | * Clinical worsening is defined as one of the following: (1) Hospitalization due to a cardiopulmonary indication, (2) Lung transplantation, (3) Death from any cause, or (4) Decrease in 6MWD of at least 15% from baseline (at 2 consecutive visits at least 24 hours apart), directly related to disease

PH-ILD Phase 2 Study Met Primary Objective of Safety and Tolerability, With Lower Rates of Treatment Discontinuation and SAEs vs. Placebo

Trial was randomized 3:1 TPIP vs. placebo

	TPIP (N=29)	Placebo (N=10)
Dose Titration % Patients Titrated to Maximum 640 µg Dose of TPIP or Placebo (n) % Patients Titrated to at least 480 µg Dose of TPIP or Placebo (n)	 79.3% (23) 89.6% (26)	 100.0% (10) 100.0% (10)
% Patients with Any TEAE (n)	93.1% (27)	90.0% (9)
% Patients with Study Drug Related[1] TEAE (n) % Patients with Study Drug Related Cough[2] (n)	55.2% (16) 37.9% (11)	40.0% (4) 0.0% (0)
% Patients with TEAE Leading to Treatment Discontinuation (n)	13.8% (4)	30.0% (3)
% Patients with Any SAE (n)	20.7% (6)	40.0% (4)
% Patients with Study Drug Related[1] SAE (n)	0.0% (0)	0.0% (0)
% Patient Deaths[3] (n)	6.9% (2)	20.0% (2)

TEAE: treatment emergent adverse event | SAE: serious adverse event | TPIP: treprostinil palmitil inhalation powder | PH-ILD: pulmonary hypertension due to interstitial lung disease | N/n: number of patients | [1] Based on investigator's evaluation | [2] All events of cough were mild, and none led to treatment discontinuation. | [3] Includes any death that occurred on or after the first dose date. All deaths in the trial were related to disease progression or comorbid causes and none were attributed to TPIP.

PH-ILD Phase 2 Exploratory Efficacy Endpoints Support Advancement Into Phase 3

Trial was randomized 3:1 TPIP vs. placebo

	TPIP (N=29)		Placebo (N=10)	
	Week 16	**n**	**Week 16**	**n**
6-Minute Walk Distance (6MWD) Treatment effect (TPIP vs. placebo) at Week 16[1] (m) Confidence interval P-value	30 [-49.0, 171.0] 0.3484	29	N/A	10
NT-proBNP concentrations (pg/mL)[2] (Baseline concentrations) Geometric mean ratio to Baseline (Geometric SD)	197.50 (242.90) 0.81 (3.36)	24	382.59 (338.43) 1.13 (1.50)	7
% Patients with Clinical Worsening Event (n) P-value (TPIP vs. placebo)[3]	10.3% (3) 0.0164	29	50.0% (5)[4]	10
% Patients hospitalized due to cardiopulmonary indication (n)	0.0% (0)	29	30.0% (3)	10
% Patients with decrease in 6MWD ≥ 15% from Baseline (n)	3.4% (1)	29	20.0% (2)	10
% Patients who died from any cause (n)	6.9% (2)	29	20.0% (2)	10

PH-ILD: pulmonary hypertension due to interstitial lung disease | TPIP: treprostinil palmitil inhalation powder | 6MWD: 6-minute walk distance | N/n: number of patients | pg/mL: picograms per milliliter | [1] Calculation based on Hodges-Lehmann Estimate Location Shift | [2] Calculation based on geometric mean | [3] Calculation based on Fisher's Exact Test | [4] Two placebo patients each experienced two events, but this analysis counted only one event per subject

TPIP: Change From Baseline in Small and Large Blood Vessels

Lung imaging results from the Phase 2 PH-ILD study

	Baseline, mean (SD)		Change from baseline, %		Effect size,[a] %	*P* value
	TPIP (n=9)	Placebo (n=5)	TPIP (n=9)	Placebo (n=5)		
BV5A (mL) volume of pulmonary arteries <5 mm^2	19.5 (7.3)	33.6 (21.1)	+14.0	–7.5	+13.0	0.24
BV5A PR (%) volume of small arteries (<5 mm^2) as a fraction of total pulmonary vessel volume	24.1 (5.0)	27.6 (8.2)	+8.4	–5.5	+13.7	**0.02**
BV5A PRA (%) volume of small arteries (<5 mm^2) as a fraction of total pulmonary artery volume	44.4 (8.1)	47.1 (13.2)	+8.0	–3.8	+13.6	**0.05**
BV10A (mL) volume of pulmonary arteries >10 mm^2	11.9 (6.5)	15.8 (6.4)	–7.1	+16.3	–25.7	0.14
BV10A PR (%) volume of large arteries (>10 mm^2) as a fraction of total pulmonary vessel volume	14.0 (4.3)	14.6 (5.2)	–10.8	+16.4	–23.2	0.08
BV10A PRA (%) volume of large arteries (>10 mm^2) as a fraction of total pulmonary artery volume	25.7 (7.0)	25.0 (8.5)	–12.0	+18.7	–24.8	0.07
BV5A:BV10A RATIO	2.0 (1.1)	2.6 (2.5)	+31.4	–10.5	+49.4	0.17

There was a consistent increase of blood volume in small arteries observed with TPIP vs. placebo

SD: standard deviation | TPIP: treprostinil palmitil inhalation powder | BV5A: volume of pulmonary arteries smaller than 5 mm^2 in cross-sectional area | BV10A: volume of pulmonary arteries larger than 10 mm^2 in cross-sectional area | PH-ILD: pulmonary hypertension due to interstitial lung disease | n: number of patients | [a] Effect size was calculated as a percentage of the treatment effect divided by the placebo arm baseline mean.

TPIP: Change From Baseline in High Attenuation Abnormality Score[a]

Lung imaging results from the Phase 2 PH-ILD study

	Change from baseline, mean (SD)		Effect size,[c] %	*P* value
	TPIP (n=9)	Placebo (n=5)		
HAA score,[b] %	–0.7 (2.7)	0.3 (1.8)	–10.5	0.54

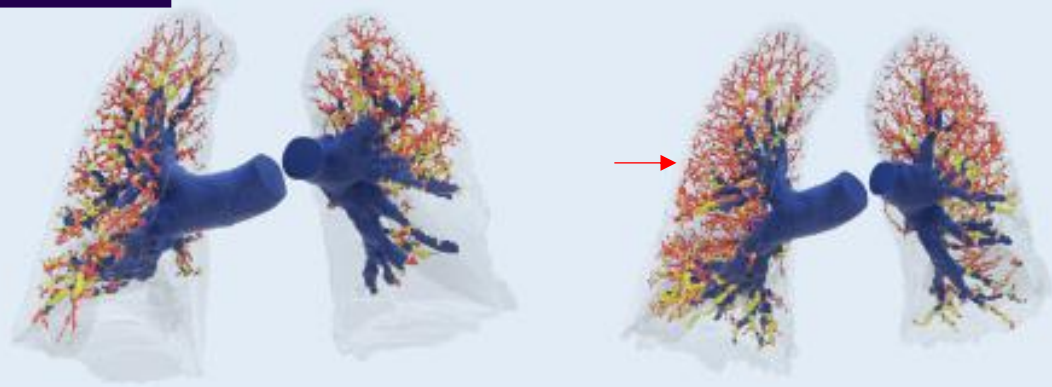
A numerical decrease from baseline in the HAA score observed with TPIP and slight increase with placebo

HAA: high-attenuation abnormality | SD: standard deviation | TPIP: treprostinil palmitil inhalation powder PH-ILD: pulmonary hypertension due to interstitial lung disease | N/n: number of patients | [a] A deep-learning algorithm was trained to distinguish between patches of voxels from scans of subjects with IPF and healthy subjects using automatically extracted high-attenuation textural features, excluding segmented blood vessels and airway walls, and to output a probability that a given patch is "fibrotic." The algorithm is applied to overlapping patches, calculating the attenuation probability for a given voxel as an average probability of all the patches which cover that voxel. The HAA score is that volume of high-attenuation voxels with a greater than 50% chance of being "fibrotic." | [b] The HAA score is expressed as a percentage of total lung volume. | [c] Effect size was calculated as a percentage of the treatment effect divided by the placebo arm baseline mean.

TPIP: FRI in Representative Patients Treated With TPIP (A) vs. Placebo (B)

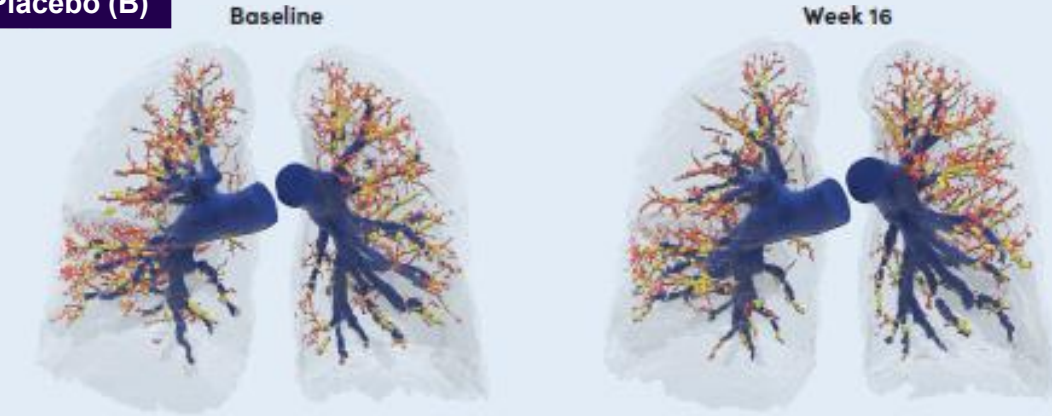
Lung imaging results from the Phase 2 PH-ILD study

TPIP (A)



TPIP	Change from baseline, mL (%)
BV5A:BV10A RATIO	+0.45 (+29.7%)

Placebo (B)



Placebo	Change from baseline, mL (%)
BV5A:BV10A RATIO	-0.11 (-8%)

Color indicates vessel size. Small vessels with cross-sectional area (CSA) <5 mm2 are colored in red (●), vessels with CSA 5-10 mm2 – in yellow (●), and CSA >10 mm2 – in blue (●). Parameters indicated as BV5 and BV10 represent the total volume of vessels with CSA <5 mm2 and >10 mm2, respectively. Note the increase of small vessels colored in red (●) in patients treated with TPIP at week 16, compared with placebo.

- TPIP treatment resulted in a **significant increase in the fraction of blood volume in small arteries** and a directional **improvement in small-to-large artery volume ratio** versus placebo
- Results suggestive of **small vessel vasodilation** and **improved pulmonary arteriole recruitment**
- A numerical **decrease in HAA score** was observed with TPIP

- Limitations included the small sample size, which may limit the generalizability of the results and may increase the risk of random variation
- Further evaluation of FRI in a larger trial may provide additional insights and support the strength and potential increased generalizability of these findings

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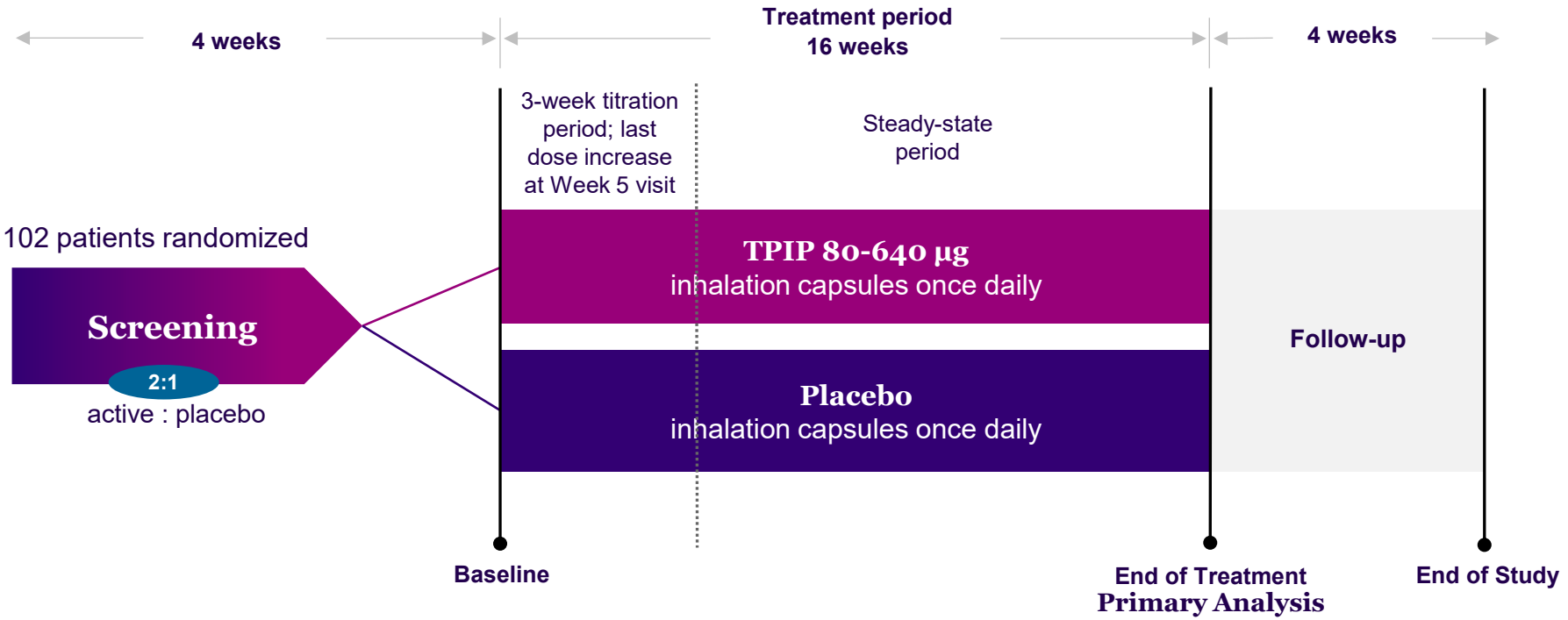
FRI: functional respiratory imaging | CSA: cross-sectional area | BV5A: volume of pulmonary arteries smaller than 5 mm^2 in cross-sectional area | BV10A: volume of pulmonary arteries larger than 10 mm^2 in cross-sectional area | TPIP: treprostinil palmitil inhalation powder | HAA: high-attenuation abnormality | PH-ILD: pulmonary hypertension due to interstitial lung disease

TPIP Phase 2b in PAH

NCT05147805 Trial summary



PAH Trial (Week 16)

Primary Endpoint

- Change from baseline in pulmonary vascular resistance (PVR)*

Secondary Endpoints

- Change from baseline in exercise capacity (6MWD)*
- Change from baseline in biomarkers of cardiac stress (NT-proBNP)*
- Pharmacokinetics

Exploratory Endpoints

- Proportion of patients that improved WHO Functional Class
- Change from baseline Cardiac Index (CI)*
- Change from baseline in Quality of Life (CAMPHOR questionnaire)

TPIP: treprostinil palmitil inhalation powder | PAH: pulmonary arterial hypertension | PVR: pulmonary vascular resistance | 6MWD: 6-minute walk distance | NT-proBNP: N-terminal pro-B-type natriuretic peptide | WHO: World Health Organization | CI: Cardiac Index | * measured approximately 24 hours after prior dose

Baseline Characteristics Reasonably **Well-Balanced** Across Study Arms

	TPIP (N=69)	Placebo (N=33)	Total (N=102)
Age: Mean, years (SD)	48.1 (15.00)	46.9 (15.22)	47.7 (15.00)
Age < 65 years, % (n)	75.4 (52)	87.9 (29)	79.4 (81)
Sex: Female, % (n)	84.1 (58)	78.8 (26)	82.4 (84)
BMI: Mean, kg/m^2 (SD)	26.746 (4.8690)	27.050 (4.8296)	26.844 (4.8344)
Geographic Region, % (n)			
USA	13.0 (9)	9.1 (3)	11.8 (12)
Europe	37.7 (26)	33.3 (11)	36.3 (37)
Japan	11.6 (8)	6.1 (2)	9.8 (10)
Rest of the World	37.7(26)	51.5 (17)	42.2 (43)
WHO Functional Class*, % (n)			
Class II	65.2 (45)	66.7 (22)	65.7 (67)
Class III	34.8 (24)	33.3 (11)	34.3 (35)
Number of Baseline PAH Medications*, % (n)			
0 or 1**	23.2 (16)	12.1 (4)	19.6 (20)
2	76.8 (53)	87.9 (29)	80.4 (82)
PAH Subtype, % (n)			
Idiopathic	72.5 (50)	69.7 (23)	71.6 (73)
Heritable	4.3 (3)	6.1 (2)	4.9 (5)
Connective Tissue Disease-Associated	21.7 (15)	21.2 (7)	21.6 (22)
Congenital Heart Disease-Related	1.4 (1)	3.0 (1)	2.0 (2)
Pulmonary Vascular Resistance			
Mean PVR, Wood Units (SD)	9.588 (5.0072)	11.069 (5.9400)	10.067 (5.3427)
Mean PVR, dyn·s·cm^{-5} (SD)	751.33 (401.421)	856.83 (464.290)	785.46 (423.376)
6-Minute Walk Distance			
Mean 6MWD, meters (SD)	348.48 (79.791)	371.06 (60.571)	355.78 (74.576)

TPIP: treprostinil palmitil inhalation powder | PAH: pulmonary arterial hypertension | BMI: body mass index | WHO: World Health Organization | N/n: number of patients | PVR: pulmonary vascular resistance | 6MWD: 6-minute walk distance | * stratification factor | ** All patients were on at least one stable background medication

TPIP Generally **Well-Tolerated** With a **Low Discontinuation Rate**

	TPIP (N=69)	Placebo (N=33)	Total (N=102)
Dose Titration, % (n)*			
Titrated to at least 480 µg	84.1 (58)	84.8 (28)	
Titrated to max dose of 640 µg	75.4 (52)	81.8 (27)	
Participants Completed the Study, % (n)			
Completed	89.9 (62)	100.0 (33)	93.1 (95)
Discontinued	10.1 (7)	0	6.9 (7)
Reason for Discontinuation:			
Adverse Event	5.8 (4)	0	3.9 (4)
Physician Decision	1.4 (1)	0	1.0 (1)
Withdrawal of Subject	2.9 (2)	0	2.0 (2)

TPIP Participants

75%

Reached study max dose of 640 µg

90%

Completed the 16-week study

95% of the 95 patients that completed the trial have **enrolled in the OLE** study

OLE patients may titrate up to a max daily **dose of 1,280 µg**

TPIP: treprostinil palmitil inhalation powder | OLE: open-label extension | N/n: number of patients | * Dose level achieved at end of dosing interval (Week 5 visit)

PVR: Highly Statistically Significant Primary Endpoint Achieved With Once-Daily Therapy (P<0.001*)

	TPIP (N=69)		Placebo (N=33)	
	Week 16	n	Week 16	n
Primary Endpoint				
Pulmonary Vascular Resistance				
PVR at Baseline:				
Mean PVR, Wood Units (SD)	9.588 (5.0072)	69	11.069 (5.9400)	33
PVR at Week 16:				
Mean PVR, Wood Units	6.218	62	10.019	33
LS Mean Ratio to Baseline†	0.63	69	0.97	33
Placebo-Adjusted Mean Ratio to Baseline PVR†:				
Ratio of LS Mean Ratio to Baseline	0.65			
[95% Confidence Interval]	[0.54, 0.79]			
P-value	<0.001			

35%* *Placebo-Adjusted Reduction in PVR† at Week 16*

Results showcase **strong treatment effect** when evaluated **~24 hours after** prior dose was administered

n: number of patients | TPIP: treprostinil palmitil inhalation powder | PVR: pulmonary vascular resistance | LS: least-squares | WHO: World Health Organization | * statistically significant at Week 16 | † Analysis performed using an ANCOVA model, adjusting for treatment group, baseline pulmonary vascular resistance (PVR), and randomization stratification factors. The model was applied to log-transformed PVR values, which were then back-transformed to the original scale.

Exercise Capacity: TPIP Showed a Clear Improvement in 6MWD (P=0.003*)

	TPIP (N=69)		Placebo (N=33)	
	Week 16	n	Week 16	n
Secondary Endpoint				
6-Minute Walk Distance				
6MWD at Baseline (m): Mean (SD)	348.48 (79.791)	69	371.06 (60.571)	33
6MWD at Week 16 (m): Mean (SD)	405.13 (98.497)	61	382.61 (91.148)	33
Absolute Change from Baseline 6MWD (m): Mean (SD)	49.71 (66.197)	61	11.55 (65.167)	33
Median	41.50		20.50	
Placebo-Adjusted Improvement from Baseline 6MWD† (m): [95% Confidence Interval]	35.49 [11.23, 60.73]	69		
P-value*	0.003			

All Efficacy Endpoints
Measured ~24 Hours After Dose

+35.5
meters

Placebo-Adjusted Improvement in 6MWD† at Week 16

n: number of patients | TPIP: treprostinil palmitil inhalation powder | 6MWD: 6-minute walk distance | * Nominal p-value not adjusted for multiplicity | † Covariate-adjusted estimate of location shift. Analysis performed using a rank ANCOVA model, adjusting for treatment group, baseline 6-minute walk distance (6MWD), and randomization stratification factors

Cardiac Stress: TPIP Showed a Meaningful Reduction in NT-proBNP (P<0.001*)

	TPIP (N=69)		Placebo (N=33)	
	Week 16	n	Week 16	n
Secondary Endpoint				
NT-proBNP Concentration				
Concentration at Baseline (pg/mL): Mean	785.58	69	798.91	33
Concentration at Week 16 (pg/mL): Mean	342.40	62	1180.14	33
LS Mean Ratio to Baseline† (pg/mL)	0.48	67	1.22	33
Placebo-Adjusted Mean Ratio to Baseline NT-proBNP†: Ratio of LS Mean Ratio to Baseline	0.40			
[95% Confidence Interval]	[0.27, 0.59]			
P-value*	<0.001			

All Efficacy Endpoints
Measured ~24 Hours After Dose

60%

Placebo-Adjusted Reduction in NT-proBNP Concentrations† at Week 16

TPIP: treprostinil palmitil inhalation powder | NT-proBNP: N-terminal pro-B-type natriuretic peptide | LS: least-squares | n: number of patients | pg/mL: picograms per milliliter | * Nominal p-value not adjusted for multiplicity | † Analysis performed using a repeated measures mixed model, adjusting for treatment group, baseline NT-proBNP, randomization stratification factors, visit and treatment-by-visit interaction. The model was applied to log-transformed NT-proBNP values, which were then back-transformed to the original scale.

WHO Functional Class: More Patients on TPIP Achieved an Improvement in Functional Class

	TPIP (N=69)		Placebo (N=33)	
	Week 16	n	Week 16	n
Exploratory Endpoint				
WHO Functional Class Shift, %				
FC Improvement* at Week 16:	30.4	21	15.2	5
FC II Improvement to FC I	13.0	9	6.1	2
FC III Improvement to FC II or FC I:	17.4	12	9.1	3
Improvement to FC II	15.9	11	9.1	3
Improvement to FC I	1.4	1	0	0
Odds Ratio for TPIP vs. Placebo†:	2.566			
[95% Confidence Interval]	[0.834, 7.890]			
P-value**	0.098			

— FC Improvement —

Week 16 vs. Baseline

TPIP **30%** ***vs.*** ***Placebo*** **15%**

Represents at Least One Functional Class Improvement

n: number of patients | TPIP: treprostinil palmitil inhalation powder | PAH: pulmonary arterial hypertension | FC: functional class | * Includes at least one functional class improvement achieved at Week 16 | ** Nominal p-value not adjusted for multiplicity † Analysis performed using Cochran-Mantel-Haenszel (CMH) test, stratified by randomization factors.

Cardiac Index: TPIP Showed an Increase Compared to Placebo (P=0.006*)

	TPIP (N=69)		Placebo (N=33)	
	Week 16	n	Week 16	n
Exploratory Endpoint				
Cardiac Index, L/min/m²				
Cardiac Index at Baseline: Mean	2.641	69	2.691	33
Cardiac Index at Week 16: Mean	3.070	62	2.777	33
LS Mean Ratio to Baseline†	1.12	69	0.98	33
Placebo-Adjusted Mean Ratio to Baseline Cardiac Index†: Ratio of LS Mean Ratio to Baseline [95% Confidence Interval] P-value*	1.15 [1.04, 1.27] 0.006			

TPIP
— Cardiac Index —

15%

Increase in CI Achieved vs. Placebo at Week 16

TPIP: treprostinil palmitil inhalation powder | LS: least-squares | CI: cardiac index | PAH: pulmonary arterial hypertension | n: number of patients | † Analysis performed using an ANCOVA model, adjusting for treatment group, baseline cardiac index, and randomization stratification factors. The model was applied to log-transformed cardiac index values, which were then back-transformed to the original scale. | * Nominal p-value not adjusted for multiplicity

Safety: Most Common TPIP TEAEs Were Consistent With Known Profile of Inhaled Treprostinil

	TPIP (N=69)		Placebo (N=33)	
	Week 16	n	Week 16	n
Safety				
TEAEs, %				
Any TEAE	88.4	61	75.8	25
Serious TEAE	7.2	5	3.0	1
Severe TEAE	5.8	4	3.0	1
TEAE Leading to Treatment Discontinuation	5.8	4	0	0
Death	0	0	0	0
Most Common TEAEs Reported, %*				
Cough	40.6	28	21.2	7
Headache	31.9	22	15.2	5
Fatigue	10.1	7	3.0	1
Chest Discomfort	8.7	6	0	0
Flushing	8.7	6	3.0	1
Upper Respiratory Tract Infection	7.2	5	3.0	1
Non-Cardiac Chest Pain	5.8	4	3.0	1
Cough Severity, %				
Cough:	40.6	28	21.2	7
Mild	34.8	24	18.2	6
Moderate	5.8	4	3.0	1
Cough Leading to Treatment Discontinuation *(Moderate)*	1.4	1	0	0

TPIP — Incidence — of Cough

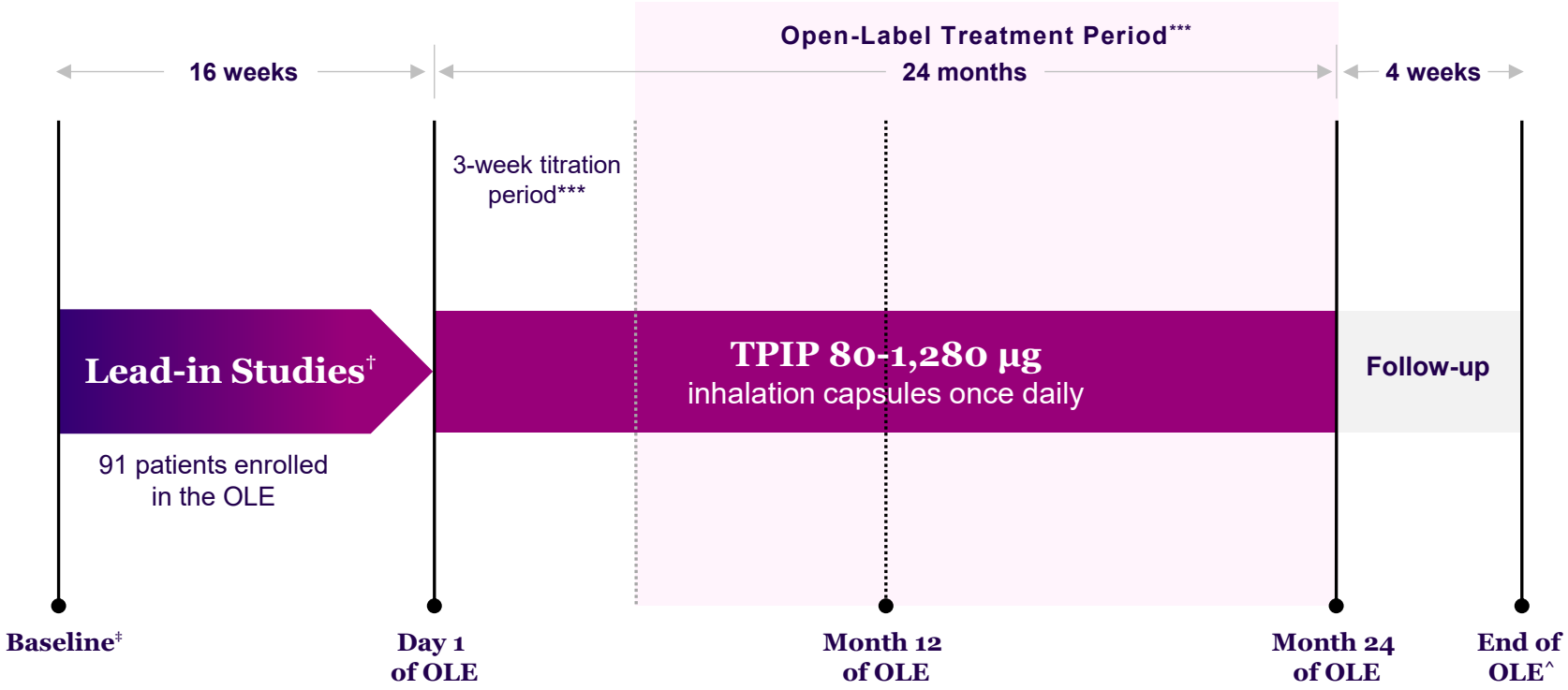
All cough incidences were reported as **mild or moderate**

>85% of cough incidences were reported as **mild**

TPIP: treprostinil palmitil inhalation powder | TEAE: treatment-emergent adverse event | PAH: pulmonary arterial hypertension | n: number of patients | * TEAEs that occurred in >5% of the treatment group and were elevated compared to placebo group

Open-Label Extension Intended to Evaluate TPIP's **Long-Term Safety & Tolerability** Over 24 Months

NCT05649748



Key OLE Study Endpoints

Primary Endpoint

- Safety and tolerability (frequency & severity of TEAEs)

Secondary Endpoints

- Change from baseline in exercise capacity (6MWD)*
- Change from baseline in biomarkers of cardiac stress (NT-proBNP)*
- Proportion of patients that improved WHO Functional Class vs. baseline
- Change from baseline REVEAL Lite 2.0 Score**

Exploratory Endpoints

- Proportion of patients who achieve a REVEAL Lite 2.0 Low Risk status
- Proportion of patients with improvement in the REVEAL Lite 2.0 Risk status

OLE: open-label extension | PAH: pulmonary arterial hypertension | TPIP: treprostinil palmitil inhalation powder | TEAE: treatment-emergent adverse event | 6MWD: 6-minute walk distance | WHO: World Health Organization | NT-proBNP: N-terminal pro-B-type natriuretic peptide | PVR: pulmonary vascular resistance | * Measured approximately 24 hours after prior dose was administered | ** A simplified, non-invasive medical tool used to estimate the mortality and disease progression risk for adult patients with PAH | *** Double-dummy titration was used to maintain blinding and permit patients who received TPIP in the lead-in studies ("TPIP Continued") to receive their achieved dose of TPIP at the start of the OLE. Patients who received placebo in the lead-in study ("Placebo Crossed") or had delayed rollover underwent titration starting at 80 µg once daily up 640 µg or highest tolerated dose. After Week 3, most patients maintained a stable TPIP dose. Investigators are permitted to titrate up to 1,280 µg to optimize treatment benefit after Week 3 of the study. | † Lead-in studies include the Phase 2b study (NCT05147805), which contributed 90 patients, and the Phase 2a 24-hour PVR study (NCT04791514), which contributed 1 patient (study was discontinued). Pre-randomization baseline values are not available for the single PVR study participant. | ‡ OLE study outcomes were evaluated against the Phase 2b lead-in study pre-randomization baseline values for relevant measurements | ^ Patients located in Japan will remain in the OLE for 84 months in accordance with Japan-specific protocol

Baseline† Characteristics Were Comparable Across Groups

	Continued TPIP[1] N=60	Placebo Crossed[2] N=31	Total N=91
Age: Mean, years	47.9	47.6	47.8
Sex: Male, % (n)	13.3% (8)	19.4% (6)	15.4% (14)
Geographic Region: % (n)			
United States	10.0% (6)	9.7% (3)	9.9% (9)
Europe	36.7% (22)	35.5% (11)	36.3% (33)
Rest of World	53.3% (32)	54.8% (17)	53.8% (49)
PAH Subtype (Idiopathic)*: % (n)	66.7% (40)	67.7% (21)	67.0% (61)
PAH Medications*: % (n)			
1	23.3% (14)	9.7% (3)	18.7% (17)
2	75.0% (45)	90.3% (28)	80.2% (73)
6MWD*: Mean (SD), meters	355.1 (79.00)	369.5 (61.73)	360.1 (73.48)
NT-proBNP*: Mean (SD), pg/mL	787.5 (1,193.2)	795.8 (1,042.1)	790.4 (1,137.5)
WHO Functional Class*: % (n)			
Class II	61.7% (37)	67.7% (21)	63.7% (58)
Class III	36.7% (22)	32.3% (10)	35.2% (32)
REVEAL Lite 2.0 Status*: % (n)			
Low (Score ≤5)	51.7% (31)	58.1% (18)	53.8% (49)
Refined Low (Score ≤4)	35.0% (21)	51.6% (16)	40.7% (37)
Intermediate (Score 6-7)	25.0% (15)	22.6% (7)	24.2% (22)
High (Score ≥8)	21.7% (13)	19.4% (6)	20.9% (19)

PAH: pulmonary arterial hypertension | 6MWD: 6-minute walk distance | NT-proBNP: N-terminal pro-B-type natriuretic peptide | WHO: World Health Organization | REVEAL Lite 2.0 risk calculator is a simplified, non-invasive medical tool used to estimate the mortality and disease progression risk for adult patients with PAH | N/n: number of patients | pg/mL: picograms per milliliter | [1] Includes all rollover patients randomized to TPIP in the Phase 2b study (NCT05147805) and 1 participant from Phase 2a 24-hour PVR study (NCT04791514) | [2] Includes all rollover patients randomized to placebo in Phase 2b study | * Single participant from the Phase 2a 24-hour PVR study had missing baseline data | † All baseline characteristics presented reflect values from both lead-in studies unless otherwise noted | Note: WHO Functional Class and number of baseline medications were stratification factors in the Phase 2b lead-in study's prespecified statistical analysis plan (SAP) | Note: All patients were on at least one background PAH medication

TPIP Was Generally **Safe** and **Well-Tolerated;** No Newly Identified Safety Signals Through Month 12

SAFETY	Total (N=91) %	Total (N=91) n
Any TEAE	89.0%	81
≤640 µg Max Dose Achieved	86.1%	62
>640 µg Max Dose Achieved**	89.5%	17**
Serious	18.7%	17
≤640 µg Max Dose Achieved	20.8%	15
>640 µg Max Dose Achieved**	10.5%	2**
Study Drug Related	1.1%	1†
Leading to Death	4.4%	4‡
Severe	16.5%	15
Leading to Study Discontinuation***	7.7%	7
Leading to Dose Reduction	11.0%	10
Study Drug Related	35.2%	32

MOST COMMON TEAEs*, % (n)

Headache	28.6%	(26)	Dizziness	6.6%	(6)
Cough	15.4%	(14)	Epistaxis	6.6%	(6)
Nasopharyngitis	14.3%	(13)	Nausea	6.6%	(6)
Diarrhea	11.0%	(10)	Anemia	5.5%	(5)
Upper Respiratory Tract Infection	9.9%	(9)	Influenza	5.5%	(5)
Bronchitis	7.7%	(7)	Pneumonia	5.5%	(5)

All TEAEs of cough were classified as **mild** or **moderate**, with **>85% being mild**

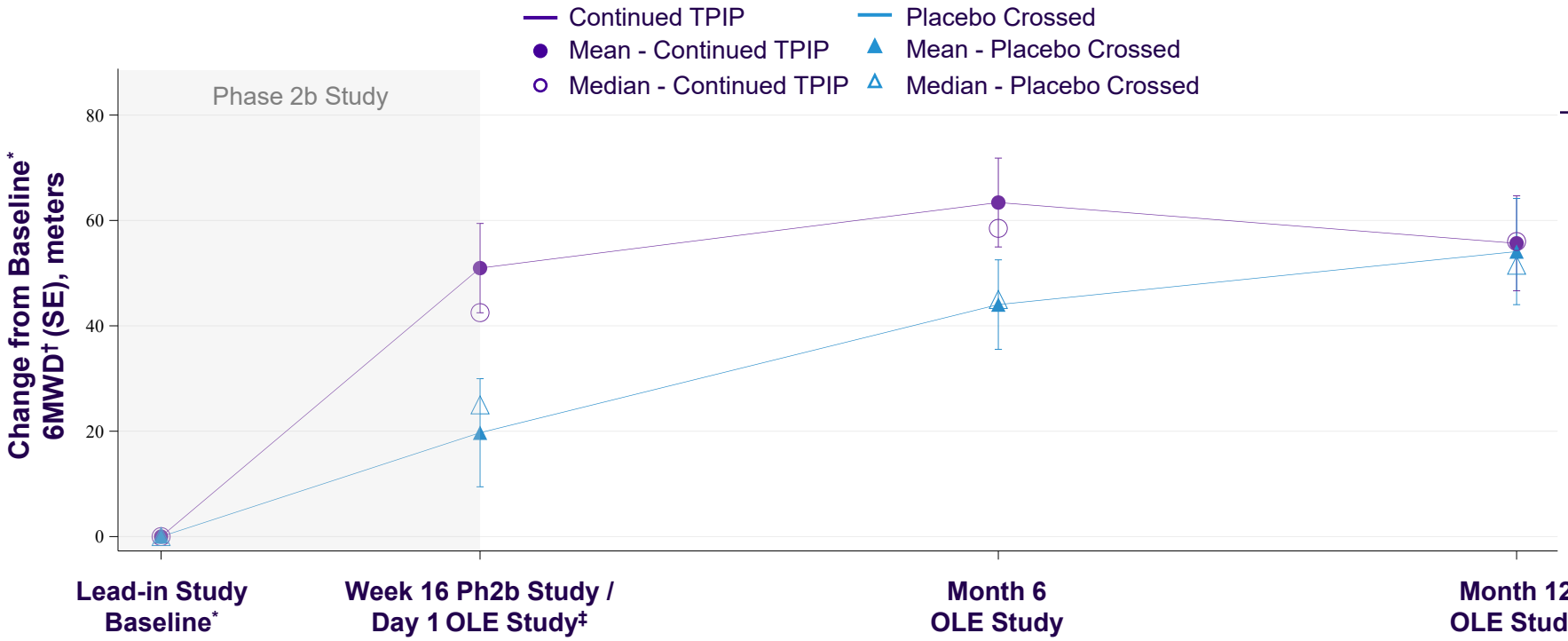
None of the 4 deaths were considered study drug related

>640 µg Max Dose Achieved by Month 12

- ✓ 19 patients (21%) achieved >640 µg dose
- ✓ No deaths or study drug related SAEs; No TEAEs led to study discontinuation**
- ✓ Only 1 cough TEAE was reported**

TPIP: treprostinil palmitil inhalation powder | TEAE: treatment-emergent adverse event | SAE: serious adverse event | OLE: open-label extension | PAH: pulmonary arterial hypertension | * TEAEs reported in ≥5% of patients | ** Includes patients whose max tolerated dose exceeded 640µg and whose adverse event occurred at a dose level that exceeded 640µg | ***All patients who discontinued treatment also discontinued study | † Patient from the Phase 2b lead-in study was hospitalized with orthostatic hypotension and subsequently discharged after precautionary workup was completed (patient discontinued their anti-hypertensive agent). Primary investigator assessed this event as study drug related | ‡ Location of participant deaths: 1 Argentina (myocardial infarction), 2 Philippines (acute respiratory failure, hypovolemic shock), 1 United States (single patient from the Phase 2a 24-hour PVR study died of acute respiratory distress syndrome in the setting of pneumonia during titration period after being off TPIP therapy for ~18 months) | Note: TEAEs reported in this table are only those that emerged during the OLE, not during the lead-in studies

Patients that Continued on TPIP Showed **Sustained Improvement** in 6MWD Over 12 Months



Mean Improvement from Baseline* 6MWD at Month 12

Continued TPIP

+55.7 *meters*

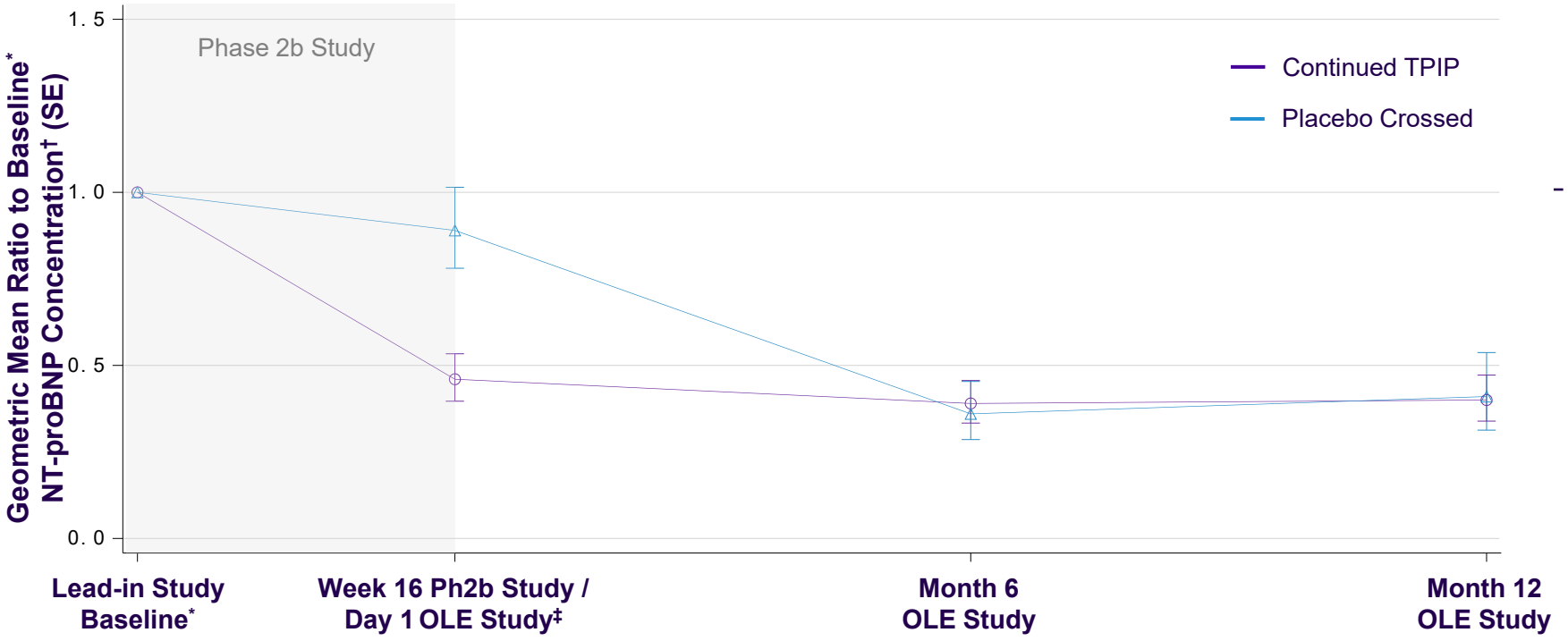
Placebo Crossed

+54.1 *meters*

Patients who crossed from **placebo to TPIP** achieved 6MWD improvement outcomes **nearly in-line** with those of continuing TPIP patients at Month 12

TPIP: treprostinil palmitil inhalation powder | 6MWD: 6-minute walk distance, measured approximately 24 hours after prior dose was administered | OLE: open-label extension | SE: standard error | Ph: phase | * Phase 2b lead-in study pre-randomization baseline values. Phase 2a 24-hour PVR study single patient data were not included in change from baseline analysis as no baseline was available. | † Last observation carried forward (LOCF) is used to impute the missing values at each visit | ‡ Day 1 OLE values are the same as the Phase 2b lead-in study Week 16 values for patients who rolled over into the OLE study within 7 days of completion.

Patients that Continued on TPIP Showed **Sustained Reduction** in NT-proBNP Over 12 Months



Mean Reduction from Baseline* NT-proBNP Concentration at Month 12

Continued TPIP

~60%

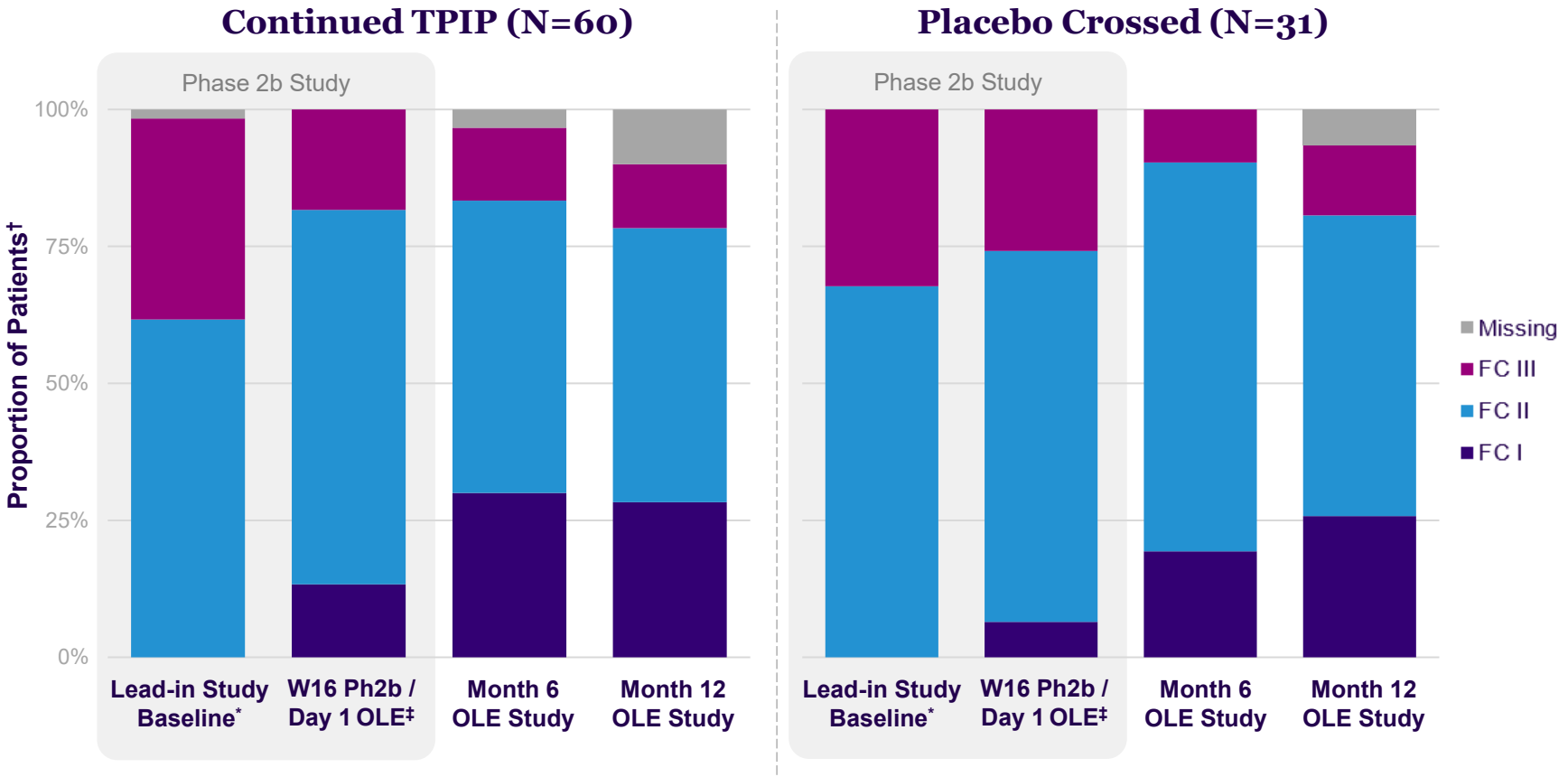
Placebo Crossed

~60%

Patients from **both groups** achieved an ~60% mean reduction in NT-proBNP levels by **Month 6** and maintained these levels at **Month 12**

TPIP: treprostinil palmitil inhalation powder | NT-proBNP: N-terminal pro-B-type natriuretic peptide, measured approximately 24 hours after prior dose was administered | OLE: open-label extension | SE: standard error | Ph: phase | * OLE study outcomes were evaluated against the Phase 2b lead-in study pre-randomization baseline value for relevant measurements | † Last observation carried forward (LOCF) is used to impute the missing value at each visit | ‡ Day 1 values are the same as the Phase 2b lead-in study Week 16 values for patients who rolled over into the OLE within 7 days of completion. | Note: Phase 2a 24-hour PVR study single patient data were not included in change from baseline analysis as no baseline was available

Both Groups Showed **Meaningful Improvement** in WHO Functional Class (FC) by Month 12



Functional Class
by Month 12

- **>25%** of all patients achieved **FC I**
  - FC I indicates **no limits** on physical activity
- **~80%** of all patients achieved **FC I or II**

50% of patients in the Continued TPIP group and **42%** of the Placebo Crossed group improved by **at least one FC category by Month 12**

TPIP: treprostinil palmitil inhalation powder | WHO: World Health Organization | FC: functional class | W: week | Ph: phase | N: number of patients | OLE: open-label extension | *OLE study outcomes were evaluated against the Phase 2b lead-in study pre-randomization baseline value for relevant measurements | † Figure proportions are based on the number of patients in the full analysis set within that treatment group including patients with missing data | ‡ Day 1 values are the same as the Phase 2b lead-in study Week 16 values for patients who rolled over into the OLE within 7 days of completion. | Note: Phase 2a 24-hour PVR single patient did not have baseline data for WHO Functional Class

REVEAL Lite 2.0 Score: Simplified, Non-Invasive, Validated Tool to Estimate the Mortality Risk of PAH Patients

Scoring[1,2]	Points	Estimated Mortality Risk	Estimated Morbidity Risk[3]
High Risk	≥ 8	>10% at 1 year	
Intermediate Risk	6 – 7	~5-10% at 1 year	
Low Risk	≤ 5	~1-5% at 1 year	~12% at 1 year
Refined Low Risk[4]	*≤ 4*	*<5% at 1 & 3 years*	*~7% at 1 year*

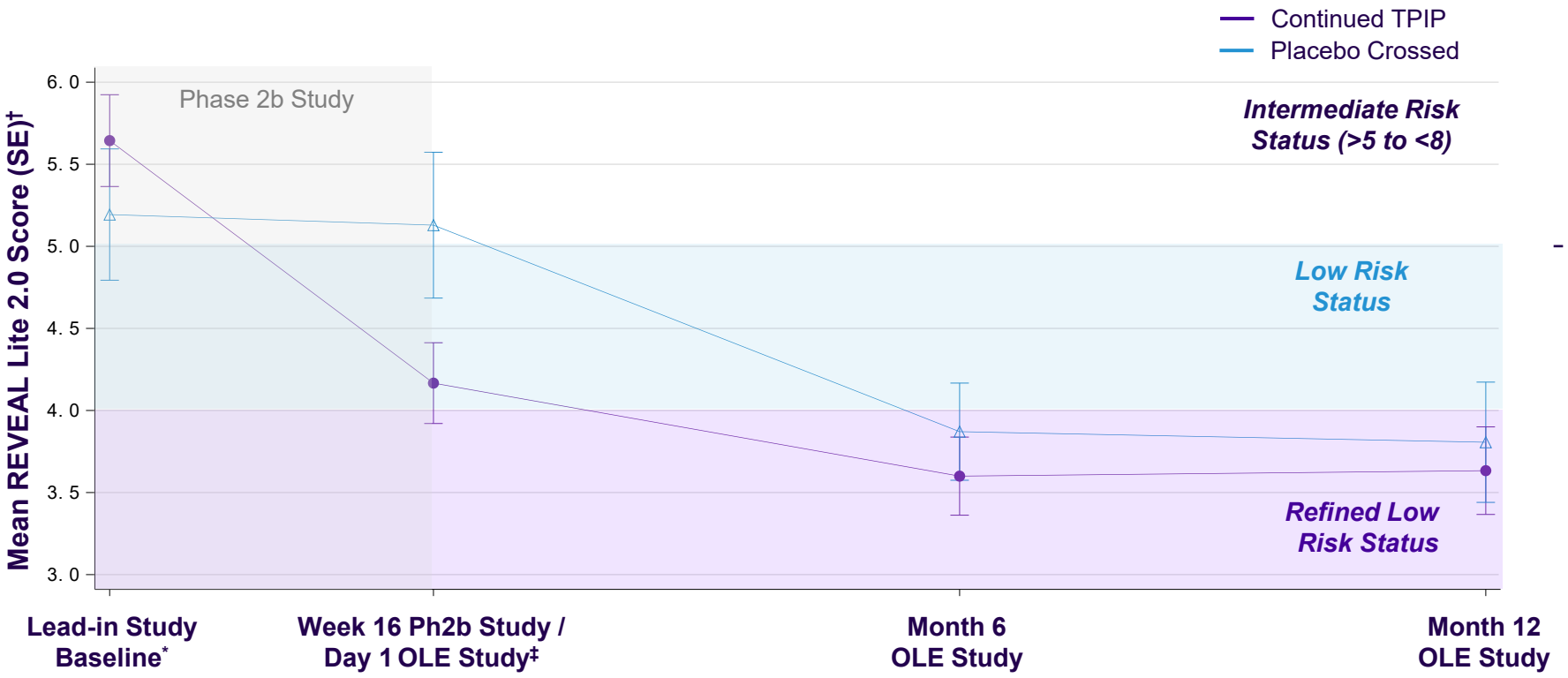
A **1-point improvement** from baseline REVEAL score is associated with a **~23% reduction** in **risk of death** and **~21% reduction** in **clinical worsening (morbidity)**[1,2,3]

Scoring Components†

- **BNP / NT-proBNP Concentration***
- **NYHA / WHO Functional Class***
- **6-Minute Walk Distance Test***
- **Systolic Blood Pressure**
- **Heart Rate**
- **Renal Insufficiency**

PAH: pulmonary arterial hypertension | NT-proBNP: N-terminal pro-B-type natriuretic peptide (BNP); a biomarker of cardiac stress | WHO: World Health Organization | NYHA: New York Heart Association | [1] Benza RL, Boucly, A., Farber, HW, et al, "Change in REVEAL Lite 2 risk score predicts outcomes in patients with pulmonary arterial hypertension in PATENT study." Journal of Heart and Lung Transplantation, 2022, 41(3), 412-420 | [2] Benza RL, Gomberg-Maitland M, Elliott, CG et al, "Development and validation of an abridged version of the REVEAL Lite 2.0 Risk Score Calculator, REVEAL Lite 2, for use in patients with pulmonary arterial hypertension. Chest 2021; 159 (1); 337-346 | [3] Morbidity, or clinical worsening, is defined by any of the following: lung transplantation, hospitalization for PAH, initiation of long-term oxygen therapy, 15% decrease in 6-minute walking distance (6MWD) from baseline with a worsening of NYHA Functional Class, or the addition of a new PAH medication. | [4] Fauvel, C., Correa Jaque, P, Liu Y, Lee SW, et al, "Refining the definition for "Low Risk" in Pulmonary Arterial Hypertension – Time to reduce morbidity and mortality." JACC: Heart failure, 2026 | † A minimum of three scoring components (variables) are required to generate a score where at least two are most predictive variables (denoted by *)

Both Groups Showed **Clinically Meaningful Improvement** in Mean REVEAL Lite 2.0 Score by Month 12



REVEAL Score Improvement by Month 12

Continued TPIP

2.0 *points*

Placebo Crossed

1.4 *points*

~65%** of all patients achieved ***Refined Low Risk*** status by Month 12

TPIP: treprostinil palmitil inhalation powder | PAH: pulmonary arterial hypertension | OLE: open-label extension | SE: standard error | Ph: phase | * Phase 2b lead-in study pre-randomization baseline | ** Percentage is based on responder analysis where the denominator is the full analysis set within that treatment group | † Last observation carried forward (LOCF) is used to impute the missing value at each visit | ‡ Day 1 values are the same as the Phase 2b lead-in study Week 16 values for patients who rolled over into the OLE within 7 days of completion. | Note: The REVEAL Lite 2.0 (or REVEAL Lite 2) risk calculator is a simplified, non-invasive medical tool used to estimate the mortality and disease progression risk for adult patients with PAH. The score can be calculated if at least two of the most predictive variables and at least three variables in total are available. | Note: Phase 2a 24-hour PVR study single patient did not have baseline REVEAL data but did have Day 1 OLE observed data and LOCF imputed data for Month 6 and Month 12

TPIP Has the Potential for Clear Differentiation in PH-ILD and PAH

Potential Differentiators		TPIP	Approved Treprostinil Therapies*** Remodulin®	TYVASO® & Yutrepia®	Orenitram® & Uptravi®
Convenience*	**Method of administration**	Inhaled (dry powder)	IV or subcutaneous	Inhaled (nebulized and/or dry powder)	Oral
	Dosing frequency	**Once daily**	Continuous	4-times per day	2- or 3-times per day
Safety & Efficacy**	**Favorable tolerability for dose expansion†**	**Yes**	Yes	No	No
	Efficacy in PAH (WHO Group 1)	**Ph2 Data Support Ph3 Advancement**	Yes	Yes	Yes
	Efficacy in PH-ILD (WHO Group 3)	**Ph2 Data Support Ph3 Advancement**	No data	Yes	No data

Favorable safety profile & higher dosing may lead to improved outcomes

insmed®

TPIP: treprostinil palmitil inhalation powder | PAH: pulmonary arterial hypertension | PH-ILD: pulmonary hypertension due to interstitial lung disease | Ph: phase | * No head-to-head or convenience studies have been conducted or planned | ** Analysis based on safety and tolerability data from the Phase 2 PH-ILD study disclosed on May 6, 2024, and the Phase 2 PAH study disclosed on June 10, 2025 | † Based on most recent publicly available data | *** Yutrepia® is approved for PAH & PH-ILD. TYVASO® is approved in PAH & PH-ILD. All other listed products are approved in PAH. TYVASO: nebulized and dry-powder. Yutrepia: dry powder. Orenitram: 2-3 times per day. Uptravi: 2-times per day

Epidemiological Footnotes *(1 of 3)*

1. Internal analysis of published BE epidemiology, including internal market research and US patient level claims data analysis:
    a) Weycker, et al. Prevalence and incidence of NCFBE among US adults in 2013. Chronic Respiratory Disease. 2017
    b) BE Patient Level Claims Data Analysis. Source: swoop/ipm.ai
    c) Trinity Epidemiology Assessment; 2020 (for Japan epi)
    d) Ringausen et al 2019 Growth (Germany)
    e) Aliberti 2016; quality standards for the management of bronchiectasis in Italy
    f) Snell et al. United Kingdom; 2019
    g) Internal Insmed NCFBE market sizing EU5 report

2. Internal analysis and estimations based on internal market research and US patient level claims data analysis:
    a) Insmed Analysis 2022: Potential Undiagnosed or Misdiagnosed (with COPD, Asthma) BE patients in US estimated based on Medical Experts driven insights, applied to Patient Level Claims Data -using advanced analytics / statistical methods Potential Undiagnosed or Co-morbid (with COPD) BE patients in US derived based on internal Insmed meta-analysis of 16 epi studies that look at BE prevalence in COPD patients; Ex-US estimates are based on extrapolation of US focused claims and epi data analysis

3. Internal analysis and estimations based on published epidemiology studies:
    a) National Health Interview Survey (NHIS) Data (2021)
    b) Alshabanat A, Zafari Z, Albanyan O, Dairi M, FitzGerald JM (2015) Asthma and COPD Overlap Syndrome (ACOS): A Systematic Review and Meta Analysis. PLoS ONE 10(9): e0136065. doi:10.1371/ journal.pone.0136065
    c) OECD/European Union (2016), “Asthma and COPD prevalence”, in Health at a Glance: Europe 2016: State of Health in the EU Cycle, OECD Publishing, Paris.
    d) Hosseini, M., Almasi-Hashiani, A., Sepidarkish, M. et al. Global prevalence of asthma-COPD overlap (ACO) in the general population: a systematic review and meta-analysis. Respir Res 20, 229 (2019). https://doi.org/10.1186/s12931-019-1198-4
    e) Blanco I, Diego I, Bueno P, et al. Geographic distribution of COPD prevalence in the world displayed by Geographic Information System maps. Eur Respir J 2019; 54: 1900610 [https://doi.org/ 10.1183/13993003.00610-2019].
    f) R. de Marco et al. Eur Respir J 2012; 39:883-892. DOI: 10.1183/09031936.000611.
    g) Iwanaga T, Tohda Y. [Epidemiology of asthma in Japan]. Nihon Rinsho. 2016 Oct;74(10):1603-1608. Japanese. PMID: 30551268
    h) Massoth L, Anderson C, McKinney KA. Asthma and Chronic Rhinosinusitis: Diagnosis and Medical Management. Med Sci (Basel). 2019 Mar 27;7(4):53. doi: 10.3390/medsci7040053. PMID: 30934800; PMCID: PMC6524348.
    i) Hashimoto S, Yoshida Y, Makita N, Sorimachi R, Sugaya S, Arita Y, Hayashi N, Tashiro N, Ichinose M. Real-World Evidence on the Diagnostic and Clinical Characteristics of Asthma in Japanese Patients with COPD: The ACO Japan Cohort Study. Int J Chron Obstruct Pulmon Dis. 2023;18:37-46
    j) Awad MT, Sankari A. Asthma and COPD Overlap. [Updated 2023 Jun 11]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK592422/
    k) https://www.cdc.gov/asthma/most_recent_national_asthma_data.htm
    l) https://www.cdc.gov/copd/php/case-reporting/national-trends-in-copd.html
    m) Minakata Y, Ichinose M. [Epidemiology of COPD in Japan]. Nihon Rinsho. 2011 Oct;69(10):1721-6. Japanese. PMID: 22073563

Epidemiological Footnotes *(2 of 3)*

4. Internal analysis of published NTM epidemiology, including internal market research and US patient level claims data analysis:
    a) Jennifer Adjemian, Kenneth N Olivier, Amy E Seitz, Steven M Holland, D Rebecca Prevots: Prevalence of nontuberculous mycobacterial lung disease in U.S. Medicare beneficiaries Am J Respir Crit Care Med. 2012 Apr 15; 185(8):881-6 DOI: 10.1164/rccm.201111-2016OC
    b) Jennifer Adjemian, D Rebecca Prevots, Jack Gallagher, Kylee Heap, Renu Gupta, David Griffith: Lack of adherence to evidence-based treatment guidelines for nontuberculous mycobacterial lung disease Ann Am Thorac Soc. 2014 Jan; 11(1): 9–16 DOI: 10.1513/AnnalsATS.201304-085OC
    c) Sara E. Strollo , Jennifer Adjemian, Michael K. Adjemian, and D. Rebecca Prevots: The Burden of Pulmonary Nontuberculous Mycobacterial Disease in the United States Ann Am Thorac Soc Vol 12, No 10, pp 1458–1464, Oct 2015 DOI: 10.1513/AnnalsATS.201503-173OC
    d) https://www.kff.org/medicare/state-indicator/total-medicare-beneficiaries/?currentTimeframe=0&sortModel=%7B%22colId%22:%22Location%22,%22sort%22:%22asc%22%7D
    e) Felix C. Ringshausen, Dirk Wagner, Andrés de Roux, Roland Diel, David Hohmann, Lennart Hickstein, Tobias Welte, Jessica Rademacher: Prevalence of Nontuberculous Mycobacterial Pulmonary Disease, Germany, 2009–2014 Emerging Infectious Diseases • www.cdc.gov/eid • Vol. 22, No. 6, June 2016 DOI: http://dx.doi.org/10.3201/eid2206.151642
    f) Jonathan E Moore, Michelle E Kruijshaar, L Peter Ormerod, Francis Drobniewski , Ibrahim Abubakar: Increasing reports of non-tuberculous mycobacteria in England, Wales and Northern Ireland, 1995-2006 BMC Public Health 2010, 10:612 http://www.biomedcentral.com/1471-2458/10/612
    g) Hoefsloot, Van Ingen et al, The geographic diversity of nontuberculous mycobacteria isolated from pulmonary samples, AN NTM-NET collaborative study; 2013, European Respiratory Journal 2013 42: 1604-1613; DOI: 10.1183/09031936.00149212
    h) Kozo Morimoto , Kazuro Iwai , Kazuhiro Uchimura , Masao Okumura , Takashi Yoshiyama , Kozo Yoshimori, Hideo Ogata , Atsuyuki Kurashima , Akihiko Gemma, and Shoji Kudoh: A Steady Increase in Nontuberculous Mycobacteriosis Mortality and Estimated Prevalence in Japan Ann Am Thorac Soc Vol 11, No 1, pp 1–8, Jan 2014, DOI: 10.1513/AnnalsATS.201303-067OC

5. Internal assessment of published epidemiology and US patient level claims data analysis, including:
    a) Kirson, N. Y., Birnbaum, H. G., Ivanova, J. I., Waldman, T., Joish, V., & Williamson, T. (2011). Prevalence of pulmonary arterial hypertension and chronic thromboembolic pulmonary hypertension in the United States. Current Medical Research and Opinion, 27(9), 1763–1768. https://doi.org/10.1185/03007995.2011.604310
    b) 2019 National Audit of Pulmonary Hypertension Great Britain; Humbert M et al, “Pulmonary arterial hypertension in France: results from a national registry”, Feb 2006
    c) Ling Y, Johnson MK, Kiely DG, Condliffe R, Elliot CA, Gibbs JS, Howard LS, Pepke-Zaba J, Sheares KK, Corris PA, Fisher AJ, Lordan JL, Gaine S, Coghlan JG, Wort SJ, Gatzoulis MA, Peacock AJ. Changing demographics, epidemiology, and survival of incident pulmonary arterial hypertension: results from the pulmonary hypertension registry of the United Kingdom and Ireland. Am J Respir Crit Care Med. 2012 Oct 15;186(8):790-6. doi: 10.1164/rccm.201203-0383OC. Epub 2012 Jul 12. PMID: 22798320.
    d) Escribano-Subias P, Blanco I, López-Meseguer M, Lopez-Guarch CJ, Roman A, Morales P, Castillo-Palma MJ, Segovia J, Gómez-Sanchez MA, Barberà JA; REHAP investigators. Survival in pulmonary hypertension in Spain: insights from the Spanish registry. Eur Respir J. 2012 Sep;40(3):596-603. doi: 10.1183/09031936.00101211. Epub 2012 Feb 23. PMID: 22362843.
    e) Hoeper MM, Huscher D, Pittrow D. Incidence and prevalence of pulmonary arterial hypertension in Germany. Int J Cardiol. 2016 Jan 15;203:612-3. doi: 10.1016/j.ijcard.2015.11.001. Epub 2015 Nov 9. PMID: 26580339.
    f) Humbert M, Sitbon O, Chaouat A, Bertocchi M, Habib G, Gressin V, Yaici A, Weitzenblum E, Cordier JF, Chabot F, Dromer C, Pison C, Reynaud-Gaubert M, Haloun A, Laurent M, Hachulla E, Simonneau G. Pulmonary arterial hypertension in France: results from a national registry. Am J Respir Crit Care Med. 2006 May 1;173(9):1023-30. doi: 10.1164/rccm.200510-1668OC. Epub 2006 Feb 2. PMID: 16456139.
    g) Secondary research: Japan’s Intractable Disease Database 2021

Epidemiological Footnotes *(3 of 3)*

6. Internal assessment of published epidemiology, including:
    a) Andersen, C. U., Mellemkjær, S., Hilberg, O., Nielsen-Kudsk, J. E., Simonsen, U., & Bendstrup, E. (2012). Pulmonary hypertension in interstitial lung disease: prevalence, prognosis and 6 min walk test. Respiratory medicine, 106(6), 875-882.
    b) Ryu, Jay H., et al. "Pulmonary hypertension in patients with interstitial lung diseases." Mayo Clinic Proceedings. Vol. 82. No. 3. Elsevier, 2007
    c) Duchemann et al., “Prevalence and incidence of interstitial lung diseases in a multi-ethnic county of Greater Paris.” European Respiratory Journal, 2017
    d) Diagnosed prevalence for PH-LHD, CTEPH and PH-Idiopathic sourced from “Patient-Based Forecast Model Pulmonary Hypertension”, Datamonitor, September 2023.

7. Internal assessment of published epidemiology, including:
    a) Singer et al, “Claims-based Prevalence of Disease Progression among Patients with Fibrosing Interstitial Lung Disease Other than Idiopathic Pulmonary Fibrosis in the United States”, Annals of American Thoracis Society 2022 Jul;19(7):1112-1121. doi: 10.1513/AnnalsATS.202102-222OC
    b) EU and JPN PPF prevalence estimated based on (1:1.2) ratio given lack of robust sources on EU5/JPN

8. Internal assessment of published epidemiology, including:
    a) Perez et al, “Incidence, prevalence, and clinical course of idiopathic pulmonary fibrosis: a population-based study”, Chest 2010 Jan;137(1):129-37. doi: 10.1378/chest.09-1002
    b) Agabiti et al, “Idiopathic Pulmonary Fibrosis (IPF) incidence and prevalence in Italy”, Sarcoidosis Vasc Diffuse Lung Dis 2014 Oct 20;31(3):191-7
    c) Kreuter et al, “Epidemiology, healthcare utilization, and related costs among patients with IPF: results from a German claims database analysis”, 2022 Mar 19;23(1):62. doi: 10.1186/s12931-022-01976-0
    d) Navaratnam et al, “The rising incidence of idiopathic pulmonary fibrosis in the U.K”, Thorax, 2011 Jun;66(6):462-7. doi: 10.1136/thx.2010.148031
    e) Harari et al, “Epidemiology of idiopathic pulmonary fibrosis: a population-based study in primary care”, Intern Emerg Med, 2020 Apr;15(3):437-445. doi: 10.1007/s11739-019-02195-0. Epub 2019 Sep 20
    f) Secondary Research: Japan’s Intractable database, 2025

TPIP Footnotes *(1 of 3):*

1. Insmed Phase 2b Study of TPIP in PAH; Placebo-Adjusted Reduction from Baseline PVR at Week 16; Analysis performed using an ANCOVA model, adjusting for treatment group, baseline pulmonary vascular resistance (PVR), and randomization stratification factors. The model was applied to log-transformed PVR values, which were then back-transformed to the original scale; statistically significant, $p<0.001$; Measurements were taken at ~24 hours post dose ("at trough"); Topline results presented June 2025.

2. Insmed Phase 2b Study of TPIP in PAH; Placebo-Adjusted Improvement from Baseline 6MWD at Week 16; Covariate-adjusted estimate of location shift. Analysis performed using a rank ANCOVA model, adjusting for treatment group, baseline 6-minute walk distance (6MWD), and randomization stratification factors; Nominally statistically significant, not adjusted for multiplicity, $p=0.003$; Measurements were taken at ~24 hours post dose ("at trough"); Topline results presented June 2025.

3. Insmed Phase 2b Study of TPIP in PAH; Placebo-Adjusted Mean Ratio to baseline NT-proBNP of 0.40; Analysis performed using a repeated measures mixed model, adjusting for treatment group, baseline NT-proBNP, randomization stratification factors, visit and treatment-by-visit interaction. The model was applied to log-transformed NT-proBNP values, which were then back-transformed to the original scale; nominally statistically significant, not adjusted for multiplicity, $p<0.001$; Measurements were taken at ~24 hours post dose ("at trough"); Topline results presented June 2025.

4. Insmed OLE Study of TPIP in PAH (12-Month Analysis); Patients in the TPIP Continued group showed a mean improvement from baseline 6MWD of 55.7 meters at Month 12. Patients in the Placebo Crossed group showed a mean improvement from baseline 6MWD of 54.1 meters; Measurements were taken at ~24-hours post dose ("at trough"); The baseline values used in this OLE are from the Phase 2b study (pre-randomization values). The Phase 2a 24-hour PVR study single patient data were not included in this change from baseline analysis as no baseline data were available; Last observation carried forward (LOCF) is used to impute the missing values at each visit; Results presented July 2026.

5. Insmed OLE Study of TPIP in PAH (12-Month Analysis); Patients in the TPIP Continued group showed a mean improvement from baseline NT-proBNP concentration of 60% at Month 12. Patients in the Placebo Crossed group showed a mean reduction from baseline NT-proBNP concentration of 60%; Measurements were taken at ~24 hours post dose ("at trough"); The baseline values used in this OLE are from the Phase 2b study (pre-randomization values). The Phase 2a 24-hour PVR study single patient data were not included in this change from baseline analysis as no baseline data were available; Last observation carried forward (LOCF) is used to impute the missing values at each visit; Results presented July 2026.

6. Insmed OLE Study of TPIP in PAH (12-Month Analysis); ~80% of patients in the TPIP Continued group and the Placebo Crossed group achieved WHO Functional Class I or II at Month 12; Results presented July 2026.

7. Insmed OLE Study of TPIP in PAH (12-Month Analysis); ~65% of patients in the TPIP Continued group and the Placebo Crossed group achieved Refined Low Risk status (REVEAL Lite 2.0 Score of ≤4) at Month 12; Percentage is based on responder analysis where the denominator is the full analysis set within that treatment group; When calculating the mean REVEAL Lite 2.0 score, last observation carried forward (LOCF) methodology was used to impute the missing values at each visit. The Phase 2b lead-in study (pre-randomization values) was used as the baseline. The Phase 2a 24-hour PVR study single patient did not have baseline REVEAL data but did have Day 1 OLE observed data. LOCF was used to impute data for Month 6 and Month 12 for this patient; Results presented July 2026.

8. Insmed Phase 2b Study of TPIP in PAH; 30.4% of patients on TPIP improved WHO Functional Class by at least 1 category (vs. baseline) at Week 16 compared to 15% of patients on placebo; Topline results presented June 2025.

TPIP Footnotes *(2 of 3):*

9. Phase 3 TRIUMPH study; Hodges-Lehmann (H-L) median treatment difference in change from baseline 6MWD at 12 weeks measured at peak drug exposure (p<0.001); McLaughlin, V, Benza, R, Rubin, L. et al. Addition of Inhaled Treprostinil to Oral Therapy for Pulmonary Arterial Hypertension: A Randomized Controlled Clinical Trial. JACC. 2010 May | URL: https://doi.org/10.1016/j.jacc.2010.01.027

10. TRIUMPH OLE Study; Median changes in 6MWD at 6, 12, 18, and 24 months were 28, 31, 32, and 18 meters, respectively, for all participants, inclusive of the significant attrition in median change in walk distance for those patients who initially received the placebo; Benza RL, Seeger W, McLaughlin VV, et al. Long-term effects of inhaled treprostinil in patients with pulmonary arterial hypertension: the Treprostinil Sodium Inhalation Used in the Management of Pulmonary Arterial Hypertension (TRIUMPH) study open-label extension. J Heart Lung Transplant. 2011 | URL: https://www.tyvasohcp.com/pah/efficacy-safety/triumph-extension-study/

11. Phase 3 TRIUMPH study; Hodges-Lehmann (H-L) between-treatment median difference in change from baseline NT-proBNP concentration measured at 12 weeks (p=0.0014) (ancillary endpoint); McLaughlin, V, Benza, R, Rubin, L. et al. Addition of Inhaled Treprostinil to Oral Therapy for Pulmonary Arterial Hypertension: A Randomized Controlled Clinical Trial. JACC. 2010 May | URL: https://doi.org/10.1016/j.jacc.2010.01.027

12. Phase 3 TRIUMPH study; NYHA Functional Class was a prespecified secondary endpoint but did not differ significantly between treatment and placebo at 12 weeks; McLaughlin, V, Benza, R, Rubin, L. et al. Addition of Inhaled Treprostinil to Oral Therapy for Pulmonary Arterial Hypertension: A Randomized Controlled Clinical Trial. JACC. 2010 May | URL: https://doi.org/10.1016/j.jacc.2010.01.027

13. SOTERIA OLE participants included eligible adults with PAH on stable background therapy who completed a prior sotatercept study (Phase 2 or Phase 3) without early discontinuation were enrolled. Participants received subcutaneous sotatercept (≤0.7 mg dose once every 21 days). This differs from the design of the OLE studies conducted for TYVASO and TPIP where OLE participants originated from the same lead-in (parent) study | Note on TPIP OLE: A single participant was enrolled in the OLE study from the Phase 2a 24-hour PVR study along with 90 participants from the Phase 2b study

14. Phase 2 PULSAR study; The greater degree of reduction in pulmonary vascular resistance as compared with placebo was seen at both dose levels of sotatercept, with the higher dose (0.7 mg dose) resulting in a 34% reduction from baseline. Least-squares mean difference as compared with placebo -239.5 dyn.sec.cm^{-5} (baseline 755.9 dyn.sec.cm^{-5} for high dose); Humbert, M., McLaughlin, V., Gibbs, J. S. R., Gomberg-Maitland, M., Hoeper, M. M., Preston, I. R., Souza, R., Waxman, A., Escribano Subias, P., Feldman, J., Meyer, G., Montani, D., Olsson, K. M., Manimaran, S., Barnes, J., Linde, P. G., de Oliveira Pena, J., & Badesch, D. B. (2021). Sotatercept for the treatment of pulmonary arterial hypertension. New England Journal of Medicine | URL: https://doi.org/10.1056/NEJMoa2024277

15. Phase 3 STELLAR study; Table 2. Change from Baseline at Week 24 in Primary and Secondary Efficacy End Points (Intention-to-Treat Population); The Hodges–Lehmann (H-L) estimate of the difference between the sotatercept and placebo groups in the change from baseline at week 24 in the 6-minute walk distance was 40.8 m (p<0.001); Hoeper, M. M., Badesch, D. B., Ghofrani, H. A., et al. (2023). Phase 3 trial of sotatercept for treatment of pulmonary arterial hypertension. New England Journal of Medicine 2023 | URL: https://doi.org/10.1056/NEJMoa2213558

TPIP Footnotes *(3 of 3):*

16. SOTERIA OLE study; Supplementary Table 5. Change from Baseline at Week 24 and Year 1; Mean change from baseline defined as measurement at Visit 1 of SOTERIA or the last measure from the parent study before rollover in 6MWD; Interim results of SOTERIA; Preston, I. R., Badesch, D. B., Ghofrani, H.-A., Hoeper, M. M., Channick, R. N., Chin, K. M., Humbert, M., Jing, Z.-C., Lang, I. M., McLaughlin, V. V., Simonneau, G., Souza, R., Tapson, V. F., Torres, F., White, R. J., Beaufils, B., Kim, J. B., & Rubin, L. J. (2025). A long-term follow-up study of sotatercept for treatment of pulmonary arterial hypertension: Interim results of SOTERIA. European Respiratory Journal, 2025 July | URL: https://doi.org/10.1183/13993003.01435-2024

17. Phase 3 STELLAR study; Table 2. Change from Baseline at Week 24 in Primary and Secondary Efficacy End Points (Intention-to-Treat Population); The Hodges–Lehmann (H-L) estimate of the difference between the sotatercept and placebo groups in the change from baseline at week 24 in NT-proBNP concentration was -441.6 pg/mL; Hoeper, M. M., Badesch, D. B., Ghofrani, H. A., et al. (2023). Phase 3 trial of sotatercept for treatment of pulmonary arterial hypertension. New England Journal of Medicine 2023 | URL: https://doi.org/10.1056/NEJMoa2213558

18. SOTERIA OLE study; Supplementary Table 5. Change from Baseline at Week 24 and Year 1; Mean change from baseline defined as measurement at Visit 1 of SOTERIA or the last measure from the parent study before rollover in NT-proBNP; Interim results of SOTERIA; Preston, I. R., Badesch, D. B., Ghofrani, H.A., Hoeper, M. M., Channick, R. N., Chin, K. M., Humbert, M., Jing, Z.C., Lang, I. M., McLaughlin, V. V., Simonneau, G., Souza, R., Tapson, V. F., Torres, F., White, R. J., Beaufils, B., Kim, J. B., & Rubin, L. J. (2025). A long-term follow-up study of sotatercept for treatment of pulmonary arterial hypertension: Interim results of SOTERIA. European Respiratory Journal, 2025 July | URL: https://doi.org/10.1183/13993003.01435-2024

19. Phase 3 STELLAR study; Table 2. Change from Baseline at Week 24 in Primary and Secondary Efficacy End Points (Intention-to-Treat Population); Percentage of patients with improvement from baseline WHO Functional Class 29.4% for sotatercept arm and 13.8% for placebo arm; Hoeper, M. M., Badesch, D. B., Ghofrani, H. A., et al. (2023). Phase 3 trial of sotatercept for treatment of pulmonary arterial hypertension. New England Journal of Medicine 2023 | URL: https://doi.org/10.1056/NEJMoa2213558

20. SOTERIA OLE study; Supplementary Table 5. Percent of patients in the Continued Sotatercept and Placebo-Crossed groups that achieved WHO-FC II/I by Year 1; Interim results of SOTERIA; Preston, I. R., Badesch, D. B., Ghofrani, H.-A., Hoeper, M. M., Channick, R. N., Chin, K. M., Humbert, M., Jing, Z.-C., Lang, I. M., McLaughlin, V. V., Simonneau, G., Souza, R., Tapson, V. F., Torres, F., White, R. J., Beaufils, B., Kim, J. B., & Rubin, L. J. (2025). A long-term follow-up study of sotatercept for treatment of pulmonary arterial hypertension: Interim results of SOTERIA. European Respiratory Journal, 2025 July | URL: https://doi.org/10.1183/13993003.01435-2024

Launch Analog Footnotes *(1 of 3)*

1. BRINSUPRI | Launched in Q3 2025; Q4 2025 represents the first full quarter of sales
   a) BRINSUPRI generated US$144.6 million in net product sales during the fourth quarter of 2025 (Insmed Incorporated, 2026). Insmed Incorporated. Insmed Reports Fourth-Quarter and Full-Year 2025 Financial Results and Provides Business Update. February 19, 2026. https://investor.insmed.com/2026-02-19-Insmed-Reports-Fourth-Quarter-and-Full-Year-2025-Financial-Results-and-Provides-Business-Update
   b) BRINSUPRI generated US$207.9 million in net product sales during the first quarter of 2026 (Insmed Incorporated, 2026). Insmed Incorporated. (2026, May 7). Insmed reports first-quarter 2026 financial results and provides business update. https://investor.insmed.com/2026-05-07-Insmed-Reports-First-Quarter-2026-Financial-Results-and-Provides-Business-Update
   c) BRINSUPRI generated US$309.2 million in net product sales during the second quarter of 2026 (Insmed Incorporated, 2026). Insmed Incorporated. (2026, August 6). Insmed reports second-quarter 2026 financial results and provides business update.
2. WINREVAIR | Launched in Q2 2024
   a) WINREVAIR generated US$70 million in sales during the second quarter of 2024 (Merck & Co., Inc., 2024). Merck & Co., Inc. (2024, July 30). Merck announces second-quarter 2024 financial results. https://www.merck.com/news/merck-announces-second-quarter-2024-financial-results/
   b) WINREVAIR generated US$149 million in sales during the third quarter of 2024 (Merck & Co., Inc., 2024). Merck & Co., Inc. (2024, October 31). Merck announces third-quarter 2024 financial results. https://www.merck.com/news/merck-announces-third-quarter-2024-financial-results/
   c) WINREVAIR generated US$200 million in sales during the fourth quarter of 2024 (Merck & Co., Inc., 2025). Merck & Co., Inc. (2025, February 4). Merck announces fourth-quarter and full-year 2024 financial results. https://www.merck.com/news/merck-announces-fourth-quarter-and-full-year-2024-financial-results/
   d) WINREVAIR generated US$280 million in sales during the first quarter of 2025 (Merck & Co., Inc., 2025). Merck & Co., Inc. (2025, April 24). Merck announces first-quarter 2025 financial results. https://www.merck.com/news/merck-announces-first-quarter-2025-financial-results/
3. OHTUVAYRE | Launched in Q3 2024; Q4 2024 represents the first full quarter of sales
   a) Ohtuvayre generated US$36.6 million in net product sales during the fourth quarter of 2024 (Verona Pharma plc, 2025). Verona Pharma plc. (2025, February 27). Verona Pharma reports fourth quarter and full year 2024 financial results and provides corporate update. https://www.veronapharma.com/news/verona-pharma-reports-fourth-quarter-and-full-year-2024-financial-results-and-provides-corporate-update/
   b) Ohtuvayre generated US$71.3 million in net product sales during the first quarter of 2025 (Verona Pharma plc, 2025). Verona Pharma plc. (2025, April 29). Verona Pharma reports first quarter 2025 financial results and provides corporate update. https://www.veronapharma.com/news/verona-pharma-reports-first-quarter-2025-financial-results-and-provides-corporate-update/
   c) Ohtuvayre generated US$102.9 million in net product sales during the second quarter of 2025 (Verona Pharma plc, 2025). Verona Pharma plc. (2025, August 6). Quarterly report (Form 10-Q) for the quarter ended June 30, 2025. U.S. Securities and Exchange Commission. https://www.sec.gov/Archives/edgar/data/1657312/000165731225000026/vrna-20250630.htm
   d) Ohtuvayre generated US$136 million in net sales during the third quarter of 2025 (Ligand Pharmaceuticals Incorporated, 2025). Ligand Pharmaceuticals Incorporated. (2025, November 6). Third quarter 2025 financial results [PDF]. https://s206.q4cdn.com/221775662/files/doc_financials/2025/q3/Q3_2025_Earnings_Release_Slides.pdf | Note: Third-quarter 2025 Ohtuvayre sales were sourced from Ligand disclosure of Verona-reported net sales; Ligand is eligible to receive low single-digit royalties on global Ohtuvayre net sales pursuant to its license agreement with Verona Pharma.

Launch Analog Footnotes *(2 of 3)*

4. DUPIXENT | Launched in Q2 2017
   a) Dupixent collaboration revenue was US$28.6 million during the second quarter of 2017 (Regeneron Pharmaceuticals, Inc., 2017). Regeneron Pharmaceuticals, Inc. (2017, August 3). Quarterly report (Form 10-Q) for the quarterly period ended June 30, 2017. U.S. Securities and Exchange Commission. https://www.sec.gov/Archives/edgar/data/872589/000153217617000027/regn-063017x10q.htm
   b) Dupixent collaboration revenue was US$89 million in the third quarter of 2017, with sales occurring almost exclusively in the United States (Regeneron Pharmaceuticals, Inc., 2017). Regeneron Pharmaceuticals, Inc. (2017, November 8). Regeneron reports third quarter 2017 financial and operating results. https://investor.regeneron.com/news-releases/news-release-details/regeneron-reports-third-quarter-2017-financial-and-operating
   c) Dupixent collaboration revenue was US$138.9 million during the fourth quarter of 2017 (Regeneron Pharmaceuticals, Inc., 2018). Regeneron Pharmaceuticals. Form 10-K, fiscal year ended December 31, 2017, filed February 8, 2018. U.S. SEC EDGAR. https://investor.regeneron.com/sec-filings/sec-filings/sec-filing/10-k/0001532176-18-000013
   d) Dupixent collaboration revenue was US$131.4 million during the first quarter of 2018 (Regeneron Pharmaceuticals, Inc., 2018). Regeneron Pharmaceuticals, Inc. (2018, May 3). Regeneron reports first quarter 2018 financial and operating results. https://investor.regeneron.com/news-releases/news-release-details/regeneron-reports-first-quarter-2018-financial-and-operating

5. FASENRA | Launched in Q4 2017; Q1 2018 represents the first full quarter of sales
   a) Fasenra generated US$21 million in product sales during the first quarter of 2018 (AstraZeneca PLC, 2018). AstraZeneca PLC. (2018, May 18). Q1 2018 results announcement [PDF]. https://www.astrazeneca.com/content/dam/az/PDF/2018/Q1-2018/Q1%202018%20Results%20announcement.pdf
   b) Fasenra generated US$65 million in product sales during the second quarter of 2018 (AstraZeneca PLC, 2018). H1 2018 Results Announcement. July 26, 2018. https://www.astrazeneca.com/content/dam/az/PDF/2018/h1-2018/H1%202018%20Results%20announcement.pdf
   c) Fasenra generated US$86 million in product sales during the first nine months of 2018 (AstraZeneca PLC, 2018). Year-to-Date and Q3 2018 Results Announcement. November 8, 2018. https://www.astrazeneca.com/content/dam/az/PDF/2018/Q3/Year-To-Date_and_Q3_2018_Results_announcement.pdf
   d) Fasenra generated US$125 million in product sales during the fourth quarter of 2018 (AstraZeneca PLC, 2019). AstraZeneca PLC. Full-Year 2018 Results Announcement. February 14, 2019. https://www.astrazeneca.com/content/dam/az/PDF/2018/full-year/Full-Year_2018_Results_announcement.pdf

6. REZDIFFRA | Launched in Q2 2024
   a) Rezdiffra generated US$14.6 million in net sales during the second quarter of 2024 (Madrigal Pharmaceuticals, Inc., 2024). Madrigal Pharmaceuticals, Inc. (2024, August 7). Madrigal Pharmaceuticals reports second quarter 2024 financial results and provides business update. https://ir.madrigalpharma.com/news-releases/news-release-details/madrigal-pharmaceuticals-reports-second-quarter-2024-financial
   b) Rezdiffra generated US$62.2 million in net sales during the third quarter of 2024 (Madrigal Pharmaceuticals, Inc., 2024). Madrigal Pharmaceuticals, Inc. (2024, November 7). Madrigal Pharmaceuticals reports third quarter 2024 financial results and provides business update. https://ir.madrigalpharma.com/news-releases/news-release-details/madrigal-pharmaceuticals-reports-third-quarter-2024-financial
   c) Rezdiffra generated US$103.3 million in net sales during the fourth quarter of 2024 (Madrigal Pharmaceuticals, Inc., 2025). Madrigal Pharmaceuticals, Inc. (2025, February 27). Madrigal Pharmaceuticals reports fourth quarter and full year 2024 financial results and provides business update. https://ir.madrigalpharma.com/news-releases/news-release-details/madrigal-pharmaceuticals-reports-fourth-quarter-and-full-year-2024
   d) Rezdiffra generated US$137.3 million in net sales during the first quarter of 2025 (Madrigal Pharmaceuticals, Inc., 2025). Madrigal Pharmaceuticals, Inc. First Quarter 2025 Financial Results. May 8, 2025. Rezdiffra net sales of $137.3M. https://ir.madrigalpharma.com/news-releases/news-release-details/madrigal-pharmaceuticals-reports-first-quarter-2025-financial

Launch Analog Footnotes *(3 of 3)*

7. TEZSPIRE | Launched in Q1 2022
   a) TEZSPIRE generated US$7 million in sales during the first quarter of 2022 (Amgen Inc., 2022). Amgen reports first quarter 2022 financial results. https://investors.amgen.com/news-releases/news-release-details/amgen-reports-first-quarter-2022-financial-results
   b) TEZSPIRE generated US$29 million in sales during the second quarter of 2022 (Amgen Inc., 2022). Amgen reports second quarter 2022 financial results. https://www.amgen.com/newsroom/press-releases/2022/08/amgen-reports-second-quarter-2022-financial-results
   c) TEZSPIRE generated US$55 million in sales during the third quarter of 2022 (Amgen Inc., 2022). Amgen reports third quarter 2022 financial results. https://www.amgen.com/newsroom/press-releases/2022/11/amgen-reports-third-quarter-2022-financial-results
   d) TEZSPIRE generated US$79 million in sales during the fourth quarter of 2022 (Amgen Inc., 2023). Amgen reports fourth quarter and full year 2022 financial results. https://investors.amgen.com/news-releases/news-release-details/amgen-reports-fourth-quarter-and-full-year-2022-financial-results

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