ASPEN Topline Results

May 28, 2024

Forward Looking Statements

This presentation contains forward-looking statements that involve substantial risks and uncertainties. "Forward-looking statements," as that term is defined in the Private Securities Litigation Reform Act of 1995, are statements that are not historical facts and involve a number of risks and uncertainties. Words herein such as "may," "will," "should," "could," "would," "expects," "plans," "anticipates," "believes," "estimates," "projects," "predicts," "intends," "potential," "continues," and similar expressions (as well as other words or expressions referencing future events, conditions or circumstances) may identify 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: the risk that the full data set from the ASPEN study or data generated in further clinical trials of brensocatib will not be consistent with the topline results of the ASPEN study; failure to obtain, or delays in obtaining, regulatory approvals for brensocatib in the U.S., Europe or Japan; failure to successfully commercialize brensocatib, if approved by applicable regulatory authorities, in the U.S., Europe or Japan, or to maintain U.S., European or Japanese approval for brensocatib once approved; uncertainties in the degree of market acceptance of brensocatib by physicians, patients, third-party payors and others in the healthcare community; inaccuracies in the Company's estimates of the size of the potential markets for brensocatib or in data the Company has used to identify physicians; expected rates of patient uptake, duration of expected treatment, or expected patient adherence or discontinuation rates; inability of the Company, Esteve Pharmaceuticals, S.A., Thermo Fisher Scientific, Inc. or the Company's other third-party manufacturers to comply with regulatory requirements related to brensocatib; the Company's inability to obtain adequate reimbursement from government or third-party payors for brensocatib or acceptable prices for brensocatib; development of unexpected safety or efficacy concerns related to brensocatib; failure to obtain regulatory approval for potential future brensocatib indications; restrictions or other obligations imposed on us by agreements related to brensocatib, including our license agreement with AstraZeneca AB, and failure to comply with our obligations under such agreements; failure to successfully conduct future clinical trials for brensocatib, including due to the Company's potential inability to enroll or retain sufficient patients to conduct and complete the trials or generate data necessary for regulatory approval, among other things; risks that the Company's clinical studies will be delayed or that serious side effects will be identified during drug development; failure of third parties on which the Company is dependent to manufacture sufficient quantities of brensocatib for commercial or clinical needs, to conduct the Company's clinical trials, or to comply with the Company's agreements or laws and regulations that impact the Company's business or agreements with the Company; the strength and enforceability of the Company's intellectual property rights or the rights of third parties; the cost and potential reputational damage resulting from litigation to which the Company may become a party, including product liability claims; changes in laws and regulations applicable to the Company's business and failure to comply with such laws and regulations; business or economic disruptions due to catastrophes or other events, including natural disasters or public health crises; and inability to repay the Company's existing indebtedness and uncertainties with respect to the Company's need and ability to access future capital.

The Company may not actually achieve the results, plans, intentions or expectations indicated by the Company's forward-looking statements because, by their nature, forward-looking statements involve risks and uncertainties because they relate to events and depend on circumstances that may or may not occur in the future. For additional information about the risks and uncertainties that may affect the Company's business, please see the factors discussed in Item 1A, "Risk Factors," in the Company's Annual Report on Form 10-K for the year ended December 31, 2023 and any subsequent Company filings with the Securities and Exchange Commission (SEC).

The Company cautions readers not to place undue reliance on any such forward-looking statements, which speak only as of the date of this presentation. The Company disclaims any obligation, except as specifically required by law and the rules of the SEC, to publicly update or revise any such statements to reflect any change in expectations or in events, conditions or circumstances on which any such statements may be based, or that may affect the likelihood that actual results will differ from those set forth in the forward-looking statements.

Please be aware that brensocatib is an investigational product that has not been approved for sale or found safe or effective by the FDA or any regulatory authority.

Opening Remarks

Will Lewis

Chair & Chief Executive Officer

ASPEN Is a Clear Win for Patients

Both Doses of Brensocatib Achieved…

- Statistically significant <0.01 p-value on primary endpoint
- Clinically meaningful reduction in exacerbations
- Statistical significance on multiple secondary endpoints
- Favorable safety and tolerability profile

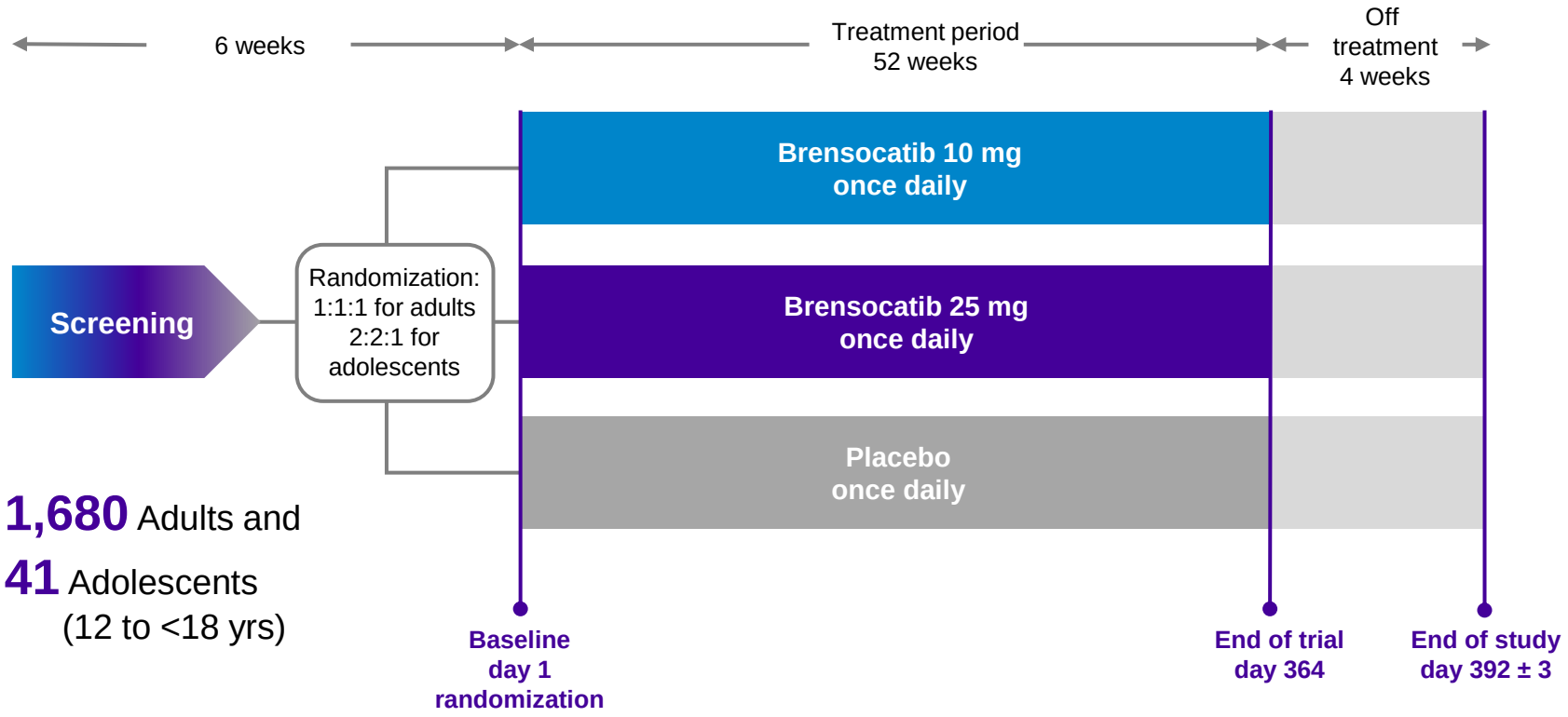
Sets Clear Path to Approval | Validates the DPP1 MoA

DPP1: Dipeptidyl peptidase 1. MoA: Mechanism of action.

ASPEN Results

Martina Flammer, M.D.
Chief Medical Officer

ASPEN is a Phase 3, Randomized, Double-Blind, Placebo-Controlled, 52-Week Study of Brensocatib



1,680 Adults and

41 Adolescents
(12 to <18 yrs)

Primary endpoint:
Rate of adjudicated pulmonary exacerbations (PEs) over 52 weeks

Secondary endpoints:
- Time-to-first PE
- Percentage PE free
- Change in FEV1
- Rate of severe PEs
- Change in QoL-B respiratory score

FEV1: Forced expiratory volume in 1 second. PE: pulmonary exacerbation. QoL-B: Quality of Life-Bronchiectasis Questionnaire.

Baseline Characteristics Were Well-Balanced Across Treatment Arms

	Brensocatib 10 mg n=583	Brensocatib 25 mg n=575	Placebo n=563
Age (years), mean ± SD	59.8 ± 15.9	60.6 ± 15.8	60.0 ± 15.4
Age ≥65 years, n (%)	277 (47.5)	302 (52.5)	260 (46.2)
Age ≥75 years, n (%)	83 (14.2)	84 (14.6)	93 (16.5)
Female sex, n (%)	385 (66.0)	360 (62.6)	362 (64.3)
White race, n (%)	431 (73.9)	430 (74.8)	405 (71.9)
BMI (kg/m^2), mean ± SD	25.5 ± 5.4	25.4 ± 5.1	25.1 ± 4.9
Chronic macrolide use, n (%)	110 (18.9)	114 (19.8)	105 (18.7)
Pseudomonas aeruginosa,* n (%)	203 (34.8)	205 (35.7)	199 (35.3)
≥3 exacerbations in previous 12 months,* n (%)	172 (29.5)	163 (28.3)	167 (29.7)
BSI, mean (SD)	7.1 (3.5)	7.1 (3.6)	7.1 (3.6)
Blood eosinophil count ≥300 cells/μL, n (%)	115 (19.7)	111 (19.3)	106 (18.8)
History of COPD, n (%)	77 (13.2)	83 (14.4)	102 (18.1)
History of asthma, n (%)	101 (17.3)	109 (19.0)	111 (19.7)

*Stratification criteria

BMI: body mass index; BSI: bronchiectasis severity index score; COPD: chronic obstructive pulmonary disease.

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 FEV1 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^

PE: pulmonary exacerbation FEV1: forced expiratory volume over 1 second QoL-B: Quality of Life-Bronchiectasis Questionnaire

* Statistically significant ^ Nominally significant p-value

TEAEs and Treatment Discontinuations Were Comparable in Brensocatib and Placebo Arms

	Brensocatib 10 mg n=582	Brensocatib 25 mg n=574	Placebo n=563
Any TEAE, n (%)	452 (77.7)	440 (76.7)	448 (79.6)
Severe TEAE, n (%)	74 (12.7)	67 (11.7)	90 (16.0)
Serious TEAE, n (%)	101 (17.4)	97 (16.9)	108 (19.2)
TEAE leading to death, n (%)	3 (0.5)	4 (0.7)	7 (1.2)
TEAE leading to treatment discontinuation, n (%)	25 (4.3)	22 (3.8)	23 (4.1)
TEAEs of special interest*, n (%)	42 (7.2)	56 (9.8)	53 (9.4)
Hyperkeratosis, n (%)	8 (1.4)	17 (3.0)	4 (0.7)
Periodontal/gingival event, n (%)	8 (1.4)	12 (2.1)	15 (2.7)
Severe infection, n (%)	4 (0.7)	7 (1.2)	4 (0.7)
Pneumonia, n (%)	23 (4.0)	27 (4.7)	33 (5.9)

Rates of TEAEs of Special Interest* Were Comparable Between Treatment Arms and Placebo

TEAE: treatment-emergent adverse event. * As reported by study investigators.

Key Opinion Leader Insights

James Chalmers, MBChB, Ph.D.

Professor and Consultant Respiratory Physician at the School of Medicine, University of Dundee, UK

Lead Investigator, ASPEN

Brensocatib Has Potential to Transform the Management of Bronchiectasis

ASPEN confirms DPP1 inhibition can have profound effects in bronchiectasis

Reduction in rate of PEs for both doses in ASPEN is clinically relevant and important

Impact on lung function decline and symptoms for 25mg dose is very exciting

DPP1: Dipeptidyl peptidase 1. PEs: pulmonary exacerbations.

Closing Remarks

Will Lewis

Chair & Chief Executive Officer

The ASPEN Study is an Historic Win for Patients with Bronchiectasis

TREATMENT WITH BRENSOCATIB COMPARED WITH PLACEBO SHOWED:

Significantly reduced annual **rate of exacerbations**

Significantly lower risk of a **first exacerbation**

Significantly more patients were **exacerbation-free**

Significantly less **lung function** decline (25 mg dose only)

Nominally significant improvement in **QOL-B scores** (25 mg dose only)

Safety and tolerability profile **similar to placebo**

Join Us Tuesday, June 4, 2024, for a Commercial Webinar

Insmed's commercial leadership will provide details on the market outlook for ARIKAYCE® (amikacin liposome inhalation suspension), brensocatib, and TPIP

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