Merck Presents New Analyses Supporting the Promising Potential of Sotatercept, its Investigational Medicine for Adults with Pulmonary Arterial Hypertension (PAH)

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Exploratory post-hoc analysis of STELLAR shows potential of sotatercept to improve cardiovascular function

Interim results from SOTERIA open-label extension study represent longest safety and efficacy analysis of sotatercept to date; safety profile of sotatercept consistent with previous studies and efficacy improvements maintained after one year of therapy

Nine Merck-sponsored abstracts in PAH featured at European Respiratory Society (ERS) International Congress 2023

RAHWAY, N.J.--(BUSINESS WIRE)-- Merck (NYSE: MRK), known as MSD outside of the United States and Canada, today announced new analyses from studies of sotatercept, Merck’s novel investigational activin signaling inhibitor biologic, for adults with pulmonary arterial hypertension (PAH) (WHO Group 1) at the European Respiratory Society (ERS) International Congress 2023. A new exploratory post-hoc analysis of right heart catheterization and echocardiography data from patients in the Phase 3 STELLAR study showed treatment with sotatercept for 24 weeks on top of background therapy reduced right heart size and improved right-ventricular (RV) function and hemodynamic status. This analysis was featured in an oral presentation, with simultaneous publication in the European Respiratory Journal. An interim analysis of the Phase 3 SOTERIA open-label extension study was also presented, representing the longest safety and efficacy analysis of sotatercept to date.
“There is an urgent need for new approaches to manage PAH, a rare, progressive, and ultimately life-threatening disease,” said Dr. Eliav Barr, senior vice president and head of global clinical development, chief medical officer, Merck Research Laboratories. “These latest data build on the clinically meaningful efficacy results from the STELLAR trial and support our belief that sotatercept has the potential to transform the treatment of PAH. PAH can strain the heart and lead to eventual right heart failure, so we are particularly encouraged by the exploratory analysis from STELLAR suggesting that treatment with sotatercept improved right heart size and function.”

Primary efficacy results from STELLAR, in which sotatercept on top of background therapy demonstrated a statistically significant and clinically meaningful improvement in 6-minute walk distance (6MWD) at 24 weeks and eight of nine secondary outcome measures, were presented at ACC.23/WCC and published in The New England Journal of Medicine. Merck submitted an application for regulatory approval of sotatercept to the U.S. Food and Drug Administration and plans to submit applications to additional regulatory agencies worldwide.

At ERS 2023, nine Merck-sponsored studies in PAH were presented. These include an oral presentation of a population health model predicting the long-term impact of sotatercept on morbidity and mortality in patients with PAH (#OA740).

Results from STELLAR hemodynamics and echocardiography analysis (Abstract #3111)

An exploratory post-hoc analysis from the STELLAR trial evaluated the effects of sotatercept on select hemodynamic parameters and right-ventricle (RV) function. The STELLAR trial enrolled 323 adults with PAH, randomized to receive sotatercept (n=163) or placebo (n=160), on top of background therapy. Participants with available data at screening and week 24 visits were included in this post-hoc analysis, which reported hemodynamic data from 298 participants and echocardiography data from 275 participants, representing 92% and 85% of total participants respectively. In the analysis, after 24 weeks, sotatercept was associated with meaningful improvements in certain measures of hemodynamic status and RV function.

Results from this exploratory analysis showed treatment with sotatercept compared to placebo, on top of background therapy, led to improvements from baseline in mean pulmonary arterial (PA) pressure (~13.9 mmHg), PA compliance (0.58 mL mmHg⁻¹), pulmonary vascular resistance (~254.8 dyn·s·cm⁻⁵), mean right atrial pressure (~2.7 mmHg), mixed venous oxygen saturation (3.84%), PA elastance (~0.42 mmHg mL⁻¹ beat⁻¹), cardiac efficiency (0.48 mL beat⁻¹ mmHg⁻¹), RV work (~0.85 g·m) and RV power (~32.70 mmHg·L min⁻¹). Echocardiography data showed improvements in the ratio of tricuspid annular plane systolic excursion to systolic pulmonary artery pressure (TAPSE/sPAP; 0.12 mm mmHg⁻¹), end-systolic and end-diastolic RV areas (~4.39 cm² and ~5.31 cm², respectively), tricuspid regurgitation and RV fractional area change (2.04% p<0.050). No significant between-group changes from baseline were seen for TAPSE, heart rate, cardiac output/index or stroke volume/stroke volume.
Despite available therapies, PAH remains incurable, with high morbidity and mortality, highlighting the urgent need for novel treatments that target new pathways,” said Dr. Vallerie McLaughlin*, professor of medicine and director, Pulmonary Hypertension Program, Division of Cardiovascular Medicine, University of Michigan in Ann Arbor. “Sotatercept is the first activin signaling inhibitor therapy and is proposed to modulate the vascular proliferation underlying PAH. Acknowledging the exploratory nature of these findings, this is the first clinical evidence suggesting that sotatercept may positively impact certain measures of right heart function and dimensions. This is encouraging and further supports the primary results from the STELLAR analysis, underscoring the potential of sotatercept to play a critical role in the treatment of PAH.”

Results from SOTERIA study (Abstract #OA739)

SOTERIA (NCT04796337) is an ongoing open-label extension study evaluating the long-term safety, tolerability and efficacy of sotatercept when added to background therapy for the treatment of PAH in patients who have completed previous sotatercept studies without early discontinuation. The primary objective of SOTERIA is to evaluate long-term safety and tolerability. The secondary objective is to assess the continued efficacy of sotatercept, as measured by 6MWD, N-terminal pro-B-type natriuretic peptide (NT-proBNP), WHO functional class (FC), pulmonary vascular resistance, overall survival, and simplified French risk score.

“The SOTERIA study provides us with important insight into the longer-term safety and efficacy of sotatercept,” said Dr. Ioana Preston, director of the Pulmonary Hypertension Center and associate professor at Tufts University School of Medicine. “These results support the potential durability of clinical benefit and safety of sotatercept for the treatment of PAH.”

At the data cutoff of April 20, 2023, there were 409 participants enrolled in SOTERIA. All participants were evaluated for safety. The median duration of exposure to sotatercept was 462 days (range: 21-1,762 days), including any exposure to sotatercept during the parent study. One hundred forty-three participants rolled over from placebo. The median duration of exposure to sotatercept in SOTERIA was 189 days.

Sotatercept was well-tolerated and the safety profile was similar to previous studies. 98.5% of participants were on treatment at the time of the interim analysis. Treatment-emergent adverse events (TEAEs) occurred in 81.7% (n=334/409) of participants. Serious TEAEs occurred in 19.3% of participants but only a small proportion lead to treatment discontinuation (1.5%; n=6/409) or death (1.0%; n=4/409). Additionally, 22.7% (n=93/409) of participants experienced a telangiectasia event, 0% had a serious telangiectasia event, 0% discontinued treatment and 1% experienced dose reductions or holds due to telangiectasia. Clinical worsening events were documented. Seven participants (1.7%) experienced nine clinical worsening events.
Improvements in clinical efficacy measures measured at week 24 in SOTERIA were maintained at one year during the open-label period. One hundred thirty-one participants who reached one year of therapy in SOTERIA were evaluated for efficacy at one year; most of these participants rolled over from the Phase 2 sotatercept studies, PULSAR and SPECTRA trials. Mean change (SD) from baseline at week 24 in 6MWD (20.2 ±66.5 m) and NT-proBNP (−374.9 ±1479.4 pg/mL) were largely maintained at one year (10.9 ±73.6 m and −227.2 ±1580.1 pg/mL, respectively). The proportion of participants who improved or maintained WHO FC II from baseline at week 24 (77.2%) was similar to that at one year (76.3%). 30.1% of participants achieved low French risk score (WHO-FC I/II, 6MWD >440 m, NT-proBNP <300 pg/mL) at week 24, and 37.4% at one year.

Changes in background PAH therapy were also documented for all participants. Of participants on any prostacyclin, 29/272 (10.7%) had prostacyclin dose decreases. Of participants on infusion prostacyclin, 22/154 (14.3%) had prostacyclin dose decreases. Of participants on other PAH therapy, 21/406 (5.2%) had other PAH therapy dose decreases and 19/406 (4.6%) had other PAH therapy dose increased. As of April 20, 2023, 8 participants had discontinued prostacyclins entirely.

Summary of Presentations

Merck-sponsored studies and analyses for PAH, sotatercept and MK-5475, an investigational inhaled soluble guanylate cyclase (sGC) stimulator, featured at ERS International Congress 2023 include:

Clinical studies

- Effects of Sotatercept on Haemodynamics and Right Heart Function: Analysis of STELLAR Trial; Marius M. Hoeper; Abstract #3111
- Sotatercept for the Treatment of PAH: An Update; Marius M. Hoeper; Abstract #807
- Late Breaking Abstract - A Long-Term Follow-Up (LTFU) Study of Sotatercept for Pulmonary Arterial Hypertension (PAH); Ioana R. Preston; Abstract #807
- A Randomized Study to Evaluate the Effects of Single-Dose MK-5475 Co-Administered with Sildenafil on Systemic Hemodynamics; Mahesh J. Patel; Abstract #PA1208

Population Health and Real-World Evidence

- Population Health Model Predicting the Long-Term Impact of Sotatercept on Morbidity and Mortality in Patients with Pulmonary Arterial Hypertension (PAH); Vallerie McLaughlin; Abstract #OA740
- Concordance between physician and patient reported presence of symptoms in patients with pulmonary arterial hypertension in the US, Europe and Japan; Rogier Klok; Abstract #PA3966
• Diagnosing pulmonary arterial hypertension in the Real World; Rogier Klok; Abstract #PA1190
• End-of-life healthcare resource utilization and costs in patients with PAH: a real-world analysis; Dominik Lautsch; Abstract #PA1195
• Health related quality of life in pulmonary arterial hypertension in the US, Europe and Japan; Rogier Klok; Abstract #PA3969

* Dr. McLaughlin is an investigator in the STELLAR trial and a paid consultant to Merck.

About pulmonary arterial hypertension (PAH)

PAH is a rare, progressive and life-threatening blood vessel disorder characterized by the constriction of small pulmonary arteries and elevated blood pressure in the pulmonary circulation. Approximately 40,000 people in the U.S. are living with PAH. The disease progresses rapidly for many patients. PAH results in significant strain on the heart, leading to limited physical activity, heart failure and reduced life expectancy. The five-year mortality rate for patients with PAH is approximately 43%.

About sotatercept

Sotatercept is an investigational, potential first-in-class activin signaling inhibitor biologic being studied for the treatment of PAH (WHO Group 1). PAH is a rare disease caused by hyperproliferation of cells in the arterial walls in the lung, leading to narrowing and abnormal constriction. In pre-clinical models, sotatercept has been shown to modulate vascular cell proliferation, reversing vascular and right ventricle remodeling.

In addition to STELLAR and SOTERIA, the sotatercept clinical development program includes multiple Phase 2 and 3 trials across a broad range of patients. Studies are underway in adult patients with PAH (WHO Group 1) at intermediate or high risk of disease progression or mortality, as well as with pulmonary hypertension due to left heart disease (WHO Group 2).

Merck acquired exclusive rights to sotatercept in the pulmonary hypertension field through the acquisition of Acceleron Pharma Inc. Sotatercept is the subject of a licensing agreement with Bristol Myers Squibb.

About MK-5475

MK-5475 is an investigational dry-powder formulation of a small-molecule stimulator of soluble guanylate cyclase (sGC), designed for inhaled delivery to the pulmonary arterial circulation through the lungs. MK-5475 may stimulate sGC in the blood vessels of the lungs, which, if occurring, relaxes and widens these blood vessels. It is currently being studied in a Phase 2/3 trial for the treatment of PAH and a Phase 2 trial for the treatment of PH associated with chronic obstructive pulmonary disease.
Merck’s focus on cardiovascular disease

Merck has a long history of making an impact in cardiovascular disease. More than 60 years ago, we introduced our first cardiovascular therapy – and our scientific efforts to understand cardiovascular-related disorders have continued. Cardiovascular disease continues to be one of the most serious health challenges of the 21st century. Approximately 18 million people across the globe die every year, and in the United States one person dies every 36 seconds from cardiovascular disease.

Advancements in the treatment of cardiovascular disease can make a critical difference for patients around the world. At Merck, we strive for scientific excellence and innovation in all stages of research, from discovery through approval and life cycle management. We work with experts throughout the cardiovascular and pulmonary community to advance research that can help improve the lives of patients globally.

About Merck

At Merck, known as MSD outside of the United States and Canada, we are unified around our purpose: We use the power of leading-edge science to save and improve lives around the world. For more than 130 years, we have brought hope to humanity through the development of important medicines and vaccines. We aspire to be the premier research-intensive biopharmaceutical company in the world – and today, we are at the forefront of research to deliver innovative health solutions that advance the prevention and treatment of diseases in people and animals. We foster a diverse and inclusive global workforce and operate responsibly every day to enable a safe, sustainable and healthy future for all people and communities. For more information, visit www.merck.com and connect with us on Twitter, Facebook, Instagram, YouTube and LinkedIn.

Forward-Looking Statement of Merck & Co., Inc., Rahway, N.J., USA

This news release of Merck & Co., Inc., Rahway, N.J., USA (the “company”) includes “forward-looking statements” within the meaning of the safe harbor provisions of the U.S. Private Securities Litigation Reform Act of 1995. These statements are based upon the current beliefs and expectations of the company’s management and are subject to significant risks and uncertainties. There can be no guarantees with respect to pipeline candidates that the candidates will receive the necessary regulatory approvals or that they will prove to be commercially successful. If underlying assumptions prove inaccurate or risks or uncertainties materialize, actual results may differ materially from those set forth in the forward-looking statements.

Risks and uncertainties include but are not limited to, general industry conditions and competition; general economic factors, including interest rate and currency exchange rate fluctuations; the impact of the global outbreak
of novel coronavirus disease (COVID-19); the impact of pharmaceutical industry regulation and health care legislation in the United States and internationally; global trends toward health care cost containment; technological advances, new products and patents attained by competitors; challenges inherent in new product development, including obtaining regulatory approval; the company’s ability to accurately predict future market conditions; manufacturing difficulties or delays; financial instability of international economies and sovereign risk; dependence on the effectiveness of the company’s patents and other protections for innovative products; and the exposure to litigation, including patent litigation, and/or regulatory actions.

The company undertakes no obligation to publicly update any forward-looking statement, whether as a result of new information, future events or otherwise. Additional factors that could cause results to differ materially from those described in the forward-looking statements can be found in the company’s Annual Report on Form 10-K for the year ended December 31, 2022 and the company’s other filings with the Securities and Exchange Commission (SEC) available at the SEC’s Internet site (www.sec.gov).

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