For Immediate Release

United Therapeutics Corporation Concludes Enrollment of the *ADVANCE OUTCOMES* Study of Ralinepag for the Treatment of Pulmonary Arterial Hypertension

Ralinepag has the potential to be the first once-a-day oral prostacyclin agonist for patients with pulmonary arterial hypertension

ADVANCE OUTCOMES *will continue to accrue clinical worsening events through the end of 2025 and top-line data is expected in the first half of 2026*

SILVER SPRING, Md. and RESEARCH TRIANGLE PARK, N.C., June 23, 2025: United Therapeutics Corporation (Nasdaq: **UTHR**), a public benefit corporation, announced the conclusion of enrollment of the phase 3 *ADVANCE OUTCOMES* study evaluating the use of an extended-release formulation of ralinepag for the treatment of pulmonary arterial hypertension (**PAH**).

The *ADVANCE OUTCOMES* study enrolled 728 participants. Clinical worsening events will be accrued through the end of 2025 and top-line data from the study is expected in the first half of 2026.

"We are excited for the potential of ralinepag to be the first once-a-day oral prostacyclin agonist, which, if successful, could fundamentally change the PAH treatment paradigm, potentially leading over time to upfront use of oral prostacyclins as a first-line therapy alongside traditional ERA and PDE-5 oral products," said **Derek Solum, Ph. D.**, Senior Director, Product Development at United Therapeutics and the lead for the *ADVANCE OUTCOMES* development program. "Our philosophy and mission drive us to relentlessly seek ways to improve patient care and achieve better treatment outcomes. We are grateful for the participants and clinical investigators who have participated in this pivotal study to help us pursue our mission."

A previous phase 2 study of ralinepag in 61 PAH participants met its primary endpoint, showing a 29.8% reduction (p=0.03) in median pulmonary vascular resistance (**PVR**) after 22 weeks of treatment with ralinepag compared with placebo.

After completing participation in the phase 2 study, 45 participants entered an open-label extension (**OLE**) study to assess the safety and tolerability of ralinepag for long-term use in patients with PAH. The OLE study reported that ralinepag continued to have a manageable side effect profile. Moreover, two years after entering the OLE study, the study reported that ralinepag significantly increased six-minute walk distance (**6MWD**) by a mean of 36.3 meters (p=0.004), and over 85% of study participants remained stable in their functional class from baseline. Additionally, hemodynamic measures taken either one or two years after entering the OLE study reported significant improvements (p=0.05) in both median PVR and mean pulmonary arterial pressure. Because the OLE portion of the phase 2 study was uncontrolled, these results need to be interpreted with caution.

Ralinepag is an investigational compound that is not approved for any use in any country.

About *ADVANCE OUTCOMES*

ADVANCE OUTCOMES is a global, multi-center, placebo-controlled phase 3 study evaluating an extended-release formulation of ralinepag, an oral, selective, potent, once-daily IP receptor agonist intended to treat pulmonary arterial hypertension. The study includes participants on approved oral background PAH therapies. Participants who complete the study have the opportunity to enroll in an open label extension study, *ADVANCE EXTENSION*.

The primary endpoint of *ADVANCE OUTCOMES* is the time to the first clinical worsening event. Secondary endpoints of the study are change from Baseline through week 28 in N-terminal prohormone of brain natriuretic peptide (**NT-proBNP**), six-minute walk distance, World Health Organization (**WHO**)/New York Heart Association (**NYHA**) functional class (**FC**), REVEAL risk score, heart rate recovery following completion of the six-minute walk test (**6MWT**), and health-related quality of life; proportion of subjects meeting NT-proBNP <300 pg/mL, 6MWD >440 meters, and WHO/NYHA FC I/II; time to all-cause mortality; time to first all-cause nonelective hospitalization; and safety and tolerability in subjects with PAH.

About PAH

PAH is a life-threatening disease that affects the blood vessels in the lungs and is characterized by increased pressure in the pulmonary arteries, which are the blood vessels leading from the heart to the lungs. The elevated pressure in the pulmonary arteries strains the right side of the heart as it pumps blood to the lungs. This eventually leads to right heart failure and, ultimately, death. PAH is characterized by structural changes in blood vessel walls, aggregation of platelets, and alteration of smooth muscle cell function. PAH affects about 500,000 individuals worldwide with around 50,000 people affected in the United States. Increases in the number of people diagnosed with the disease have been observed, but due to the rarity of the disease and the complexity of diagnosing it, only a small fraction of patients with PAH are treated.

United Therapeutics: Enabling Inspiration

At United Therapeutics, our vision and mission are one. We use our enthusiasm, creativity, and persistence to innovate for the unmet medical needs of our patients and to benefit our other stakeholders. We are bold and unconventional. We have fun, we do good. We are the first publicly-traded biotech or pharmaceutical company to take the form of a public benefit corporation (**PBC**). Our public benefit purpose is to provide a brighter future for patients through (a) the development of novel pharmaceutical therapies; and (b) technologies that expand the availability of transplantable organs.

You can learn more about what it means to be a PBC here: unither.com/pbc.

Forward-Looking Statements

Statements included in this press release that are not historical in nature are "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995. Forward-looking statements include, among others, the potential for ralinepag to become the first once-a-day oral prostacyclin agonist for patients with PAH; our plan to continue accruing clinical worsening events through the end of 2025 and provide top-line data from the *ADVANCE OUTCOMES* study in the first half of 2026; the potential for ralinepag to fundamentally change the PAH treatment paradigm, potentially leading to up front use of oral prostacyclins as a first line therapy alongside traditional ERA and PDE-5 products; and our efforts to innovate for the unmet medical needs of our patients, to benefit our other stakeholders, and to pursue our public benefit purpose of developing novel pharmaceutical therapies and technologies that expand the availability of transplantable organs. These forward-looking statements are subject to certain risks and uncertainties, such as those described in our periodic reports filed with the Securities and Exchange Commission, that could cause actual results to differ materially from anticipated results. Consequently, such forward-looking statements are qualified by the cautionary statements, cautionary language, and risk factors set forth in our periodic reports and documents filed with the Securities and Exchange Commission, including our most recent Annual Report on Form 10-K, Quarterly Reports on Form 10-Q, and Current Reports on Form 8-K. We claim the protection of the safe harbor contained in the Private Securities Litigation Reform Act of 1995 for forward-looking statements. We are providing this information as of June 23, 2025, and assume no obligation to update or revise the information contained in this press release whether as a result of new information, future events or any other reason.

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