United Therapeutics Corporation Announces FDA Filing Acceptance of New Drug Application for Ralinepag to Treat Pulmonary Arterial Hypertension

*Ralinepag has the potential to redefine the PAH treatment landscape as the first and only once-daily oral prostacyclin, if approved by the U.S. Food and Drug Administration (**FDA**)*

Ralinepag combines potent receptor affinity with continuous exposure to deliver long-term, durable efficacy and disease-mitigating outcomes

SILVER SPRING, Md. & RESEARCH TRIANGLE PARK, N.C – August 24, 2026 – United Therapeutics Corporation (Nasdaq: **UTHR**), a public benefit corporation, today announced that the FDA has accepted the New Drug Application (**NDA**) for ralinepag to treat PAH. The FDA has set a Prescription Drug User Fee Act target action date of June 24, 2027. Ralinepag has not been approved for use in any indication by the FDA and remains investigational for PAH.

"Ralinepag has the potential to make an important difference for adults living with PAH — a complex, progressive, and life-threatening disease that can severely impact daily life and lead to right heart failure," said **Martine Rothblatt, Ph.D.**, Chairperson and Chief Executive Officer of United Therapeutics. "With the NDA now accepted for review, we are one step closer to offering PAH patients a new, once-daily oral treatment. In our clinical trial, ralinepag delayed disease progression, achieved clinical improvement, and provided durability of effect over many years. We attribute these robust results to its unique chemistry and multi-pathway effects, including vasodilation and anti-proliferative and anti-inflammatory activity."

The filing was based on results from the phase 3 *ADVANCE OUTCOMES* study evaluating the safety and efficacy of ralinepag in patients with PAH. The study met its primary endpoint, with ralinepag achieving a statistically significant 55% reduction in risk of clinical worsening compared with placebo in predominantly pre-treated patients with PAH. Ralinepag also achieved statistical significance for important secondary endpoints, reducing levels of N-terminal pro-B-type natriuretic peptide (**NT-proBNP**), a critical biomarker for heart failure, and improving exercise capacity, as measured by six-minute walk distance (**6MWD**). Ralinepag improved the odds of achieving clinical improvement by 47% (p=0.015), an additional secondary endpoint. These findings were consistent across all patient subgroups, including disease etiology, 6MWD, World Health Organization Functional Class (**WHO FC**), NT-proBNP levels, and use of background therapies.

The safety profile of ralinepag was consistent with known prostacyclin-related adverse events, and no new safety signals were observed.

These data were presented as part of the Breaking News: 2026 Clinical Trial Results in Pulmonary Medicine session at the 2026 annual meeting of the American Thoracic Society, and were recently published in *The Lancet*.

About Ralinepag

Ralinepag is a highly selective and potent prostacyclin (**IP**) receptor agonist with multiple pathway effects, including vasodilatory, anti-proliferative, and anti-inflammatory effects.[1,2] It demonstrates six-fold higher binding affinity for the IP receptor than MRE-269 (selexipag's active metabolite) and achieves sustained IP receptor occupancy similar to parenteral therapy.[3-6] Ralinepag helps to restore prostacyclin signaling and activates IP receptors on pulmonary artery endothelial and smooth muscle cells to trigger the downstream conversion of ATP to cAMP.[1,7] Ralinepag is six- to eight-fold more potent at increasing in vitro cAMP levels compared with the active metabolite of selexipag.[5] Elevated intracellular cAMP acts on pathways implicated in PAH progression by promoting vasodilation and inhibiting vascular remodeling, suggesting potential for vascular protection.[1,5,7] In a phase 2 study, ralinepag significantly reduced pulmonary vascular resistance compared with placebo in PAH patients on mono (41%) or dual combination (59%) background therapy.[8]

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About ADVANCE OUTCOMES

ADVANCE OUTCOMES was a pivotal phase 3 multicenter, global, randomized, double-blind, placebo-controlled, event-driven study to evaluate the efficacy and safety of ralinepag in 687 patients with PAH. Patients who completed the study had the option to enroll in an ongoing open-label extension study, *ADVANCE EXTENSION*.

In this event-driven study, patients were randomly assigned (1:1) to receive ralinepag or placebo, in addition to their standard of care PAH-specific background therapy. Once-daily dosing was individualized and titrated based on tolerability and clinical response. No dose ceiling was specified.

The primary endpoint was time to first adjudicated clinical worsening event, defined as death, nonelective hospital admission for worsening PAH, initiation of parenteral or inhaled prostacyclin pathway agent for treatment of worsening PAH, disease progression, or unsatisfactory long-term clinical response.

Secondary endpoints included changes from Baseline to Week 28 in NT-proBNP, 6MWD, and WHO/NYHA FC; shift and proportion of patients with improved risk status, clinical improvement, health-related quality of life (SF-36) as measured by patient-reported outcomes; time to first all-cause nonelective hospitalization; time to all-cause mortality; heart rate recovery following completion of the 6MWT; and safety and tolerability.

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.

About United Therapeutics

Founded by CEO Martine Rothblatt to discover a cure for her daughter's life-threatening rare disease, pulmonary arterial hypertension, United Therapeutics transforms the treatment of rare diseases and pioneers alternatives to expand the supply of transplantable organs. From our innovative therapies to our groundbreaking manufactured organs, we are bold and unconventional. We move quickly from scientific theory to practical technologies that can save lives. As a public benefit corporation, even our legal structure reflects our commitments. We serve patients, act with integrity, create long-term shareholder value, and operate with sustainable practices that protect the future we are working to build. Visit us at www.unither.com and follow us on LinkedIn, Facebook, and Instagram.

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, statements regarding: the potential timing and outcome of the FDA’s review of our NDA for ralinepag; the potential benefits of ralinepag for PAH patients, including the prospect for ralinepag to make an important difference for adults living with PAH, and the possibility that ralinepag will offer PAH patients a new, once-daily oral treatment; and our goals of expanding the supply of transplantable organs, developing practical technologies that can save lives, creating long-term shareholder value, and operating with sustainable practices. 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 August 24, 2026, 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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