Protagonist Announces Plans to Initiate a Global Phase 3 Study for Rusfertide in Polycythemia Vera Following Interactions with the U.S. Food & Drug Administration and the European Medicines Agency

March 22, 2021

-- End-of-Phase-2 meeting with the FDA, and written comments from the EMA, support advancement of the Company's clinical development plan for rusfertide in PV --

-- Management to host conference call today at 5 p.m. EDT --

NEWARK, Calif., March 22, 2021 /PRNewswire/ -- Protagonist Therapeutics (Nasdaq: PTGX) ("Protagonist" or "the Company") announced today that the Division of Nonmalignant Hematology at the U.S. Food and Drug Administration ("FDA") has provided important feedback during an End-of-Phase 2 meeting on rusfertide (PTG-300), an investigational new treatment for polycythemia vera ("PV"). Protagonist has also received written comments from the European Medicines Agency ("EMA") supportive of the Company's pivotal clinical development plan in PV.

Based on the feedback from the FDA and EMA, Protagonist intends to initiate a global Phase 3 clinical trial of rusfertide in PV. The Phase 3 trial will be a randomized, placebo-controlled study of about 200 to 250 adult participants, including both high-risk and low-risk patients, who require frequent phlebotomy treatments with or without cytoreductive or other concomitant therapies. The primary endpoint will be the proportion of patients achieving a response, with response defined as absence of phlebotomy eligibility based on hematocrit control between weeks 20 through 32. In addition, there will a durability follow-up during weeks 32-52 of the study, after which participants will be offered open-label treatment for evaluation of long-term effects and safety. Frequency of phlebotomies, as well as symptom improvement as measured by MPN-TSS criteria, will be among the important secondary endpoints in the study.

"Rusfertide presents a unique potential treatment for the wide range of PV patients whose hematocrit remains uncontrolled by frequent phlebotomy—with or without cytoreductive agents—which thereby exposes them to significant thrombotic risks," saic Srdan Verstovsek, MD, PhD, an investigator on the Phase 2 study of rusfertide in PV and Professor in the Department of Leukemia at The University of Texas MD Anderson Cancer Center. "As a clinical investigator, I look forward to participating in this Phase 3 study, which is designed to explore rusfertide's unique hepcidin hormone mimetic mechanism to address specific and pressing unmet needs in PV."

"We are very thankful to the FDA and EMA for their expedited dialogue around this potential new treatment for PV, and we look forward to advancing our clinical development program for rusfertide based on the clear and timely guidance these regulators have provided us," said Sam Saks, MD, Chief Medical Officer of Protagonist. "Based on this End-of-Phase-2 meeting with the FDA, and the written comments from the EMA, we believe we have very good alignment on the central elements of the pivotal study. Importantly, the Phase 3 study will have endpoints and inclusion/exclusion criteria similar to those in the ongoing Phase 2 study. We believe a single Phase 3 study design, in addition to the ongoing Phase 2 study, should support a future New Drug Application and Marketing Authorisation Application in the U.S. and Europe, respectively."

Conference Call and Webcast Information

To access the live call, dial 1-844-515-9178 (U.S./Canada) or 1-614-999-9313 (International) and refer to conference ID #: 3553805. A live webcast of the call will also be accessible on the Investors section of the Company's website at www.protagonist-inc.com. The replay will be available on the company's website approximately two hours after the call and will remain available for 60 days.

About Protagonist Therapeutics

Protagonist Therapeutics is a clinical stage biopharmaceutical company with multiple peptide-based investigational new chemical entities in different stages of development. Rusfertide (PTG-300) is an injectable hepcidin mimetic in a Phase 2 proof-of-concept clinical trial for polycythemia vera, and a separate Phase 2 clinical study for hereditary hemochromatosis. PN-943 is an orally delivered, gut-restricted alpha-4-beta-7 integrin specific antagonist peptide in a 150 patient Phase 2 study for the potential treatment of inflammatory bowel disease, with ulcerative colitis as the initial targeted indication. PTG-200 is an orally delivered, gut-restricted, interleukin-23 receptor specific antagonist peptide in a Phase 2 clinical trial for Crohn's disease. Two additional second-generation oral interleukin-23 receptor antagonist candidates, PN-235 and PN-232, are in early stages of clinical development. The Company has developed a proprietary technology platform to discover and develop novel peptide-based therapeutics to address significant unmet medical needs and transform existing treatment paradigms.

Protagonist is headquartered in Newark, California. For further information, please visit www.protagonist-inc.com.

About Polycythemia Vera
Polycythemia vera is a myeloproliferative neoplasm characterized primarily by the increased production of red blood cells. Well-established treatment guidelines focus on maintaining hematocrit levels continuously below 45 percent to reduce the risk of thrombotic events. Unfortunately, current treatment options are unable to maintain hematocrit to below the 45 percent target for many patients and may be associated with serious side effects. The prevalence of polycythemia vera is approximately 44 to 57 patients per 100,000 people in the U.S. The prevalence rate in Europe is similar.

Cautionary Note on Forward-Looking Statements
This press release contains forward-looking statements for purposes of the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. Forward-looking statements include statements regarding our intentions or current expectations concerning, among other things, our plans to conduct a Phase 3 trial evaluating rusfertide for PV. In some cases, you can identify these statements by forward-looking words such as "anticipate," "believe," "may," "will," "expect," or the negative or plural of these words or similar expressions. Forward-looking statements are not guarantees of future performance and are subject to risks and uncertainties that could cause actual results and events to differ materially from those anticipated, including, but not limited to, our ability to develop and commercialize our product candidates, our ability to earn milestone payments under our collaboration agreement with Janssen, the impact of the current COVID-19 pandemic on our discovery and development efforts, our ability to use and expand our programs to build a pipeline of product candidates, our ability to obtain and maintain regulatory approval of our product candidates, our ability to operate in a competitive industry and compete successfully against competitors that have greater resources than we do, and our ability to obtain and adequately protect intellectual property rights for our product candidates. Additional information concerning these and other risk factors affecting our business can be found in our periodic filings with the Securities and Exchange Commission, including under the heading "Risk Factors" contained in our Annual Report on Form 10-K for the year ended December 31, 2020, filed with the Securities and Exchange Commission. Forward-looking statements are not guarantees of future performance, and our actual results of operations, financial condition and liquidity, and the development of the industry in which we operate, may differ materially from the forward-looking statements contained in this press release. Any forward-looking statements that we make in this press release speak only as of the date of this press release. We assume no obligation to update our forward-looking statements, whether as a result of new information, future events or otherwise, after the date of this press release.

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