Press Releases

Protagonist Announces Phase 1 and Pre-clinical Data on Hepcidin Mimetic PTG-300 Presented at European Hematology Association Annual Meeting

-- PTG-300 demonstrates pharmacodynamic clinical proof-of-concept based on sustained, dose-related reduction in serum iron in healthy volunteers --

-- Company plans to begin Phase 2 study in beta-thalassemia patients in the fourth quarter of 2018 --

NEWARK, Calif., June 18, 2018 /PRNewswire/ -- Protagonist Therapeutics, Inc. (Nasdaq: PTGX) today announced that results of a Phase 1 study in healthy volunteers and supportive pre-clinical data for the Company's novel injectable hepcidin mimetic, PTG-300, were the subject of oral presentations on June 16, 2018, at the 23rd Congress of the European Hematology Association (EHA) in Stockholm. Protagonist is developing PTG-300 for the treatment of anemia and iron overload in related rare blood disorder diseases, including beta thalassemia.

"The Phase 1 clinical results demonstrated the ability of PTG-300 to achieve a sustained, dose-related reduction in serum iron," commented Richard Shames, M.D., Chief Medical Officer at Protagonist. "This observation was evident in both single ascending and repeat doses -- a clear demonstration of pharmacodynamic-based proof-of-concept in human volunteers. In addition, the pre-clinical results with PTG-300 in a mouse model of beta-thalassemia provide proof-of-mechanism activity for the treatment of anemia and support for advancing this drug candidate into patient studies."

"These pre-clinical and clinical results demonstrate the potential of PTG-300 in the treatment of a broad range of blood disorders," added Dinesh V. Patel, Ph.D., Protagonist President and Chief Executive Officer. "We look forward to pursuing initial development of PTG-300 for the treatment of patients with beta-thalassemia who are non-transfusion dependent as well as for severely-affected patients who are dependent on transfusion. We continue to work toward initiation of an open label Phase 2 trial in the fourth quarter of 2018."

Details of EHA Presentations

- **Hepcidin Mimetic PTG-300 for Treatment of Ineffective Erythropoiesis and Chronic Anemia in Hemoglobinopathy Diseases**

  Agents with hepcidin activity may help correct iron distribution abnormalities and have beneficial effects on erythropoiesis. In a preclinical mouse model of beta-thalassemia, PTG-

300 demonstrated the ability to reduce iron toxicity for developing erythrocytes in the bone marrow, addressing a contributing factor to ineffective erythropoiesis. The ability to address ineffective erythropoiesis could lead to a potential treatment for chronic anemia in conditions characterized by low endogenous hepcidin levels and high serum iron levels, such as beta-thalassemia and myelodysplastic syndrome.

- **Hepcidin Mimetic PTG-300 Induces Dose-Related and Sustained Reductions in Serum Iron and Transferrin Saturation in Healthy Subjects**

  This first-in-human randomized, double-blind, placebo-controlled study of subcutaneous PTG-300 was conducted to evaluate safety and tolerability, pharmacokinetics and pharmacodynamic activity of PTG-300 in 62 healthy volunteers. The single-dose groups received PTG-300 over the dose range of 1-80 mg and the repeat dose cohort received 40 mg once weekly for two doses. PTG-300 demonstrated a rapid and sustained dose-related reduction in serum iron from baseline. At higher doses, maximal reduction in serum iron extended for at least 72 hours. The repeat dose administration demonstrated a comparable iron reduction following both doses. Treatment with PTG-300 was generally well tolerated and no dose-limiting toxicities or serious adverse events were reported.

About PTG-300 and Hepcidin

PTG-300, an injectable hepcidin mimetic, is currently in clinical development for the potential treatment of anemia and iron overload related to rare blood disorders. Ultimately PTG-300 also has the potential to treat secondary iron overload in such diseases by reducing the need for transfusions and by decreasing excessive dietary iron absorption. Protagonist plans to initiate a Phase 2 study of PTG-300 in patients with beta-thalassemia in Q4 2018. PTG-300 therapy may also be potentially beneficial in other diseases such as myelodysplastic syndrome (MDS), myelofibrosis, hereditary hemochromatosis (HH), polycythemia vera (PCV), siderophilic infections, and liver fibrosis which provide additional opportunities for future development. The U.S. Food Administration granted Orphan Drug Designation to PTG-300 for the treatment of beta-thalassemia in March of 2018.

Hepcidin is a natural peptide hormone that is the main regulatory hormone governing iron absorption, recycling and utilization by the body. Iron plays an essential role in various body functions, especially blood formation, but too much iron is toxic and causes anemia and organ damage over time. Abnormally low hepcidin levels, caused by genetic mutations or secondary pathology, can result in the body absorbing and storing more iron than is needed, leading to iron overload.

About Protagonist Therapeutics, Inc.

Protagonist Therapeutics is a clinical stage biopharmaceutical company that utilizes a proprietary technology platform to discover and develop novel peptide-based drugs to transform existing treatment paradigms for patients with significant unmet medical needs. PTG-100 is an oral alpha-4-beta-7 integrin antagonist peptide that is under evaluation for potential treatment of inflammatory bowel diseases. The Company's interleukin-23 receptor antagonist peptide, PTG-

200, is currently in a Phase 1 clinical trial in healthy volunteers to support a Phase 2 study in Crohn's disease. The IL-12/23 pathway blockade is an approach that has been validated through an FDA-approved injectable antibody drug. The company has entered into a worldwide license and collaboration agreement with Janssen Biotech for the clinical development of PTG-200. Protagonist has also applied its innovative peptide platform outside of gastrointestinal disease areas and is developing an injectable hepcidin mimetic, PTG-300, for the potential treatment of anemia and iron overload related to rare blood diseases with an initial focus on beta-thalassemia. The Company has completed a Phase 1 clinical trial with PTG-300, which established pharmacodynamic-based clinical proof-of-concept in normal healthy volunteers. The U.S. Food and Drug Administration has granted Orphan Drug Designation to PTG-300 for beta-thalassemia.

Protagonist is headquartered in Newark, California, with pre-clinical and clinical staff in California and discovery operations in both California and Brisbane, Queensland, Australia. For further information, please visit http://www.protagonist-inc.com.

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, the potential for our programs, our collaborations and milestone payments we may receive under them, the initiation and availability of results of our clinical trials, our research and development plans, the utility of our intellectual property, and the adequacy of our capital resources. 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, 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. We discuss many of these risks in greater detail under the heading "Risk Factors" contained in our quarterly report on Form 10-Q for the three months ended March 31, 2018 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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SOURCE Protagonist Therapeutics, Inc.

Solebury Trout; Rich Allan (media); Tel: +1 646-378-2958; Email: rallan@troutgroup.com OR Marcy Nanus (investors); Tel: +1 646-378-2927; Email: mnanus@soleburytrout.com