PsiOxus and bluebird bio Present Novel Data Combining PsiOxus T-SIGn Platform with CAR-T Therapy to Clear Primary Tumors and Metastases

- Single IV cycle of PsiOxus' T-SIGn vector enabled an otherwise non-effective dose of CAR-T cell therapy to clear primary and metastatic tumors *in vivo*
- Reprogramming of the tumor microenvironment using T-SIGn vectors could enable a variety of CAR-T therapies to overcome limitations in solid tumors
- Data is currently being presented at the AACR Virtual Annual Meeting 2021

OXFORD, UK & CAMBRIDGE, Mass./USA – 14 April 2021: PsiOxus Therapeutics, Ltd. (PsiOxus), a clinical stage oncology company re-programming the tumor microenvironment to overcome the central challenge of resistance to therapy, and bluebird bio, Inc. (Nasdaq: BLUE) presented preclinical data at the American Association for Cancer Research (AACR) Annual Meeting 2021. The study, "T-SIGn cancer gene therapy and anti-EGFR CAR-T cells synergize in combination therapy to clear A549 lung tumor xenografts", assessed anti-tumor synergy between PsiOxus' T-SIGn® vectors and an anti-epidermal growth factor receptor (EGFR) chimeric antigen receptor (CAR)-T cell therapy from bluebird bio in xenograft lung tumors.

"We are encouraged by these results showing synergistic activity between our T-SIGn vector and bluebird bio's CAR-T therapy in primary and metastatic solid tumors and are particularly excited by the ability of a single IV cycle of T-SIGn to enable an otherwise non-effective dose of CAR-T cells to clear both primary and metastatic tumors," said John Beadle, M.D., Chief Executive Officer, PsiOxus. "These data validate the potential of our T-SIGn platform to reprogram the tumor microenvironment such that CAR-T cells are recruited, activated and sustained within solid tumors to yield efficacy. We look forward to further evaluating our T-SIGn vector programs in combination with T-cell therapeutics that otherwise fail to meet their true potential to treat solid cancers."

"Cracking the solid tumor code will likely require layers of technology to reach the types of deep and durable response we aspire to as a field," said Philip Gregory, chief scientific officer, bluebird bio. "This collaboration between bluebird and PsiOxus is an example of this layered strategy, combining the power of two orthogonal anti-tumor approaches to achieve a synergistic impact on tumor control and clearance."

"Although it's early in development, we believe that this is one of the most robust data sets so far showing that an IV administered therapy is able to rewire the tumor microenvironment to enable recruitment and activation of CAR-T cells and expand the efficacy of CAR-T therapies to solid tumors, including metastases," said Brian Champion, Ph.D., Chief Scientific Officer, PsiOxus. "Results of this study validate the mechanistic foundation of our T-SIGn platform and provide a blueprint of what can be achieved as we evaluate our T-SIGn vectors in combination with additional cell therapy approaches."

The study showed that when injected intravenously into mice with established human tumor xenografts, PsiOxus' armed T-SIGn vectors reprogrammed the tumor microenvironment to a proinflammatory state. When this was followed three days later by a dose of bluebird bio's anti-EGFR CAR-T cells, two T-SIGn vectors armed with different T-cell recruitment and activation transgenes, NG-347 and NG-641, synergistically yielded anti-tumor activity. The anti-EGFR CAR-T cells demonstrated no tumor efficacy when dosed alone at the same dose and also failed to synergize with the unarmed T-SIGn vector, demonstrating that the synergy was driven by the T-SIGn vectored transgene expression within the tumor. Transcriptional analysis showed that PsiOxus' NG-347 T-SIGn vector reprogrammed the tumor microenvironment leading to enhanced activation of CAR-T cells through robust CAR-T and innate immune cell recruitment and activation, resulting in increased efficacy against both primary and metastatic tumors.

While NG-347 is a preclinical program in the IND enabling phase, NG-641 is already being evaluated in the clinic and PsiOxus plans to develop it both as a monotherapy and in combination with checkpoint inhibitors.

"This preclinical data opens up an additional valuable combination option for NG-641 to enable the effective treatment of a wide range of solid tumors with CAR-T or other cell therapies," concluded Brian Champion, Ph.D., Chief Scientific Officer, PsiOxus.

The poster, "T-SIGn cancer gene therapy and anti-EGFR CAR-T cells synergize in combination therapy to clear A549 lung tumor xenografts", is available to registered participants of the AACR Virtual Annual Meeting 2021 and can be downloaded from the PsiOxus website.

About PsiOxus
PsiOxus is a clinical stage oncology company pioneering systemic immune oncology products that drive sustained reprogramming of the tumor microenvironment to overcome the central challenge of resistance to therapy. Our validated T-SIGn® vector platform can deliver multiple transgene payloads that reengineer both primary and metastatic tumors. We have a rapidly expanding pipeline of novel monotherapy and combination products to dramatically improve outcomes for patients with cancer. For more information, please visit https://psioxus.com/.

About T-SIGn®
Tumor-Specific Immuno-Gene Therapy (T-SIGn) is a broad platform for tumor re-engineering by delivering combinations of transgenes encoding immunotherapeutic proteins. T-SIGn utilizes enadenotucirev, a chimeric group B adenovirus, as a vector system for the delivery of therapeutic transgenes to cancer cells, taking advantage of the clinically demonstrated tumor selectivity and intravenous delivery properties of this virus. The simultaneous delivery of combinations of transgenes from a single viral vector directs tumor cells to locally produce anti-cancer agents, in effect turning these cells into "drug factories" to reengineer the tumor microenvironment. The first T-SIGn candidates are aimed at promoting anti-tumor immunity: NG-350A (immune activating

antibody approach), which entered clinical trials in March 2019, and NG-641 (bispecific antibody approach targeting the tumor stroma), which entered the clinic in December 2019. Other T-SIGn candidate approaches include clinical stage NG-348 (a membrane bound ligand gene therapy) as well as preclinical programs, including in collaboration with the Parker Institute for Cancer Immunotherapy.

About bluebird bio, Inc.

bluebird bio is pioneering gene therapy with purpose. From our Cambridge, Mass., headquarters, we're developing gene and cell therapies for severe genetic diseases and cancer, with the goal that people facing potentially fatal conditions with limited treatment options can live their lives fully. Beyond our labs, we're working to positively disrupt the healthcare system to create access, transparency and education so that gene therapy can become available to all those who can benefit.

bluebird bio is a human company powered by human stories. We're putting our care and expertise to work across a spectrum of disorders including cerebral adrenoleukodystrophy, sickle cell disease, β-thalassemia and multiple myeloma using three gene therapy technologies: gene addition, cell therapy and (megaTAL-enabled) gene editing.

bluebird bio has additional nests in Seattle, Wash.; Durham, N.C.; and Zug, Switzerland. For more information, visit bluebirdbio.com.

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Forward Looking Statements

This release contains "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995, including statements regarding bluebird bio's preclinical and research programs. Any forward-looking statements are based on management's current expectations of future events and are subject to a number of risks and uncertainties that could cause actual results to differ materially and adversely from those set forth in or implied by such forward-looking statements. These risks and uncertainties include, but are not limited to, the risk that previously conducted studies involving similar product candidates will not be repeated or observed in ongoing or future studies involving current product candidates, the risk that preclinical results will not be observed in clinical trials, the risk that we will not enter into a definitive collaboration agreement with PsiOxus, and the risk that any one or more of our product candidates will not be successfully developed and commercialized. For a discussion of other risks and uncertainties, and other important factors, any of which could cause our actual results to differ from those contained in the forward-looking statements, see the section entitled "Risk Factors" in our most recent annual report on Form 10-K, as well as discussions of potential risks, uncertainties, and other important factors in our subsequent filings with the Securities and Exchange Commission. All information in this press release is as of the date of the release, and bluebird bio undertakes no duty to update this information unless required by law.

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