Circle Pharma announces publication in Journal of Medicinal Chemistry of results from collaboration with Pfizer Inc.

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South San Francisco, CA, January 17, 2018, -- Circle Pharma, Inc. today announced that results from its collaborative work with Pfizer Inc. to develop a potent and orally bioavailable macrocycle modulator of the chemokine receptor, CXCR7, have been published in the Journal of Medicinal Chemistry.

The goal of the collaboration was to deploy Circle's rational design platform for macrocycle therapeutics in order to improve the drug-like characteristics of an existing macrocycle compound, and in particular to develop a cell permeable, orally bioavailable compound with enhanced target affinity. As reported in the publication, the collaboration produced a series of permeable and potent derivative macrocycles, including a compound having >500-fold increase in potency (CXCR7 Ki of ~ 9nM versus 2 uM for the starting compound), good cell permeability and 18% oral bioavailability in rats.

Additionally, permeable CXCR7 binding compounds with novel macrocycle backbone scaffolds were discovered through the efforts of the collaboration. This finding was not described in the publication.

"Cell permeability and orally bioavailability have been long-standing and well recognized challenges in the development of macrocycle therapeutics: nearly all synthetic macrocycle compounds in clinical development are against extracellular targets and are delivered by injection," noted David J. Earp, JD, PhD, Circle's CEO. "Circle's rational design approach coupled with efficient, low-cost synthesis uniquely enables us to design cell permeable, bioavailable macrocycles to address therapeutic targets that have been out

of reach, including intracellular protein-protein interactions. This is a large target class with significant unmet clinical need."

"This collaboration successfully achieved its very challenging objective of delivering a potent and orally bioavailable macrocycle targeting CXCR7," said Spiros Liras, PhD, Vice President, Medicinal Chemistry, Pfizer.

The open-access scientific paper, entitled "Discovery of Potent and Orally Bioavailable Macrocyclic Peptide–Peptoid Hybrid CXCR7 Modulators," is available at http://pubs.acs.org/doi/10.1021/acs.jmedchem.7b01028.

About Macrocyclic Peptides Macrocyclic peptides have the potential to allow drug developers to address the large proportion of known therapeutic targets (estimated at up to 80%) that are considered undruggable with conventional small molecule or biologic modalities. In particular, there is great interest in developing macrocycles to modulate protein-protein interactions, which play a role in almost all disease conditions, including cancer, fibrosis, inflammation and infection. However, the development of macrocyclic therapeutics has been limited by the need for a greater understanding of how to develop macrocycles with appropriate pharmacokinetics, cell permeability and oral bioavailability. Circle is applying its ability to design potent macrocycles with intrinsic cell permeability and drug-like characteristics to unlock access to challenging, high value therapeutic targets that have been out of reach by other approaches.

About Circle Pharma, Inc. Circle is developing a new paradigm for macrocycle drug discovery based on rational design and synthetic chemistry. Circle's technology facilitates the design and synthesis of intrinsically cellpermeable macrocycles that can address both intra- and extra-cellular therapeutic targets, and can be delivered by oral administration. Circle's macrocycle development platform is applicable across a wide range of serious diseases; the company is initially focusing its internal development efforts on intracellular protein-protein interactions that are key drivers in cancer. Circle's founders are Prof. Matthew P. Jacobson (Chair of the Dept. of Pharmaceutical Chemistry at UC San Francisco and co-founder of Global Blood Therapeutics (NASDAQ: GBT) and Relay Therapeutics) and Prof. R. Scott Lokey (Dept. of Chemistry and Biochemistry, UC Santa Cruz and director of the UCSC Chemical Screening Center).

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