Ambagon Therapeutics Launches with $85 Million Series A to Advance Pioneering Molecular Glue Platform and Progress Pipeline

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Modular platform enables development of molecular glue stabilizers addressing intrinsically disordered proteins, a largely undrugged target class.
Initial discovery pipeline focused on high-value targets in oncology.

SAN FRANCISCO, Calif., January 06, 2022 – Ambagon Therapeutics, a biotechnology company unlocking intrinsically disordered proteins and other difficult-to-target protein classes, today announced an $85 million Series A to augment its drug discovery platform and to advance its pipeline of molecular glues.

The financing was led by Nextech Invest. Ambagon was previously seeded by RA Capital Management, Droia Ventures, Inkef Capital, AbbVie Ventures, MRL Ventures Fund, and Mission BioCapital. Investors from the seed round joined the A round, along with new investor Surveyor Capital (a Citadel company).

Many disease-relevant proteins have regions of intrinsic disorder that cannot be targeted by conventional small molecule drugs. Several thousand proteins with such intrinsically disordered regions have been identified that interact with the hub protein 14-3-3. In binding to a disordered protein region, 14-3-3 induces order, conferring druggability.

By stabilizing naturally occurring 14-3-3:client interactions, Ambagon aims to rapidly develop novel therapeutic candidates for difficult-to-drug proteins. The pipeline currently focuses on oncology, where many opportunities exist to engage currently-undruggable targets.

Ambagon was founded by world leaders in 14-3-3 biology and drugging protein-protein interactions: Michelle Arkin, Professor and Chair of Pharmaceutical Chemistry and co-Director of the Small Molecule Discovery Center at UCSF, Luc Brunsveld, Professor of Chemical Biology at the Eindhoven University of Technology (TU/e), and Ambagon Chief Technology Officer Christian Ottmann, Associate Professor of Molecular Cell and Structural Biology, TU/e.

Ambagon's seasoned leadership team includes Chief Executive Officer Scott Clarke, previously CEO of Tizona Therapeutics and Trishula Therapeutics, and Chief Scientific Officer Nancy Pryer, previously CSO at Day One Biopharmaceuticals and Chief Development Officer at Nurix Therapeutics.

"Our deep understanding of 14-3-3 biology has broad applications for drug discovery as it opens up

disordered protein regions as therapeutic targets," said Scott Clarke. "Combined with our proprietary structural insights, curated chemical library, and bespoke drug discovery tools, our experienced drug development team is well placed to bring forward new medicines addressing previously undruggable targets."

"Ambagon's modular approach for leveraging 14-3-3 biology to enable drug discovery is not just unique, but uniquely well-conceived," said Melissa McCracken, Partner, Nextech Invest. "We are excited to see such an exciting platform translate into a very rich pipeline."
"We are proud to continue to support Ambagon as it works to create first-in-class and best-in-class drugs through targeted stabilization of protein complexes," said Adam Rosenberg, Ambagon's Chair and RA Capital Venture Partner. "Since our seed investment, the team has developed an impressive proprietary dataset and systemic understanding of 14-3-3 interactions. Ambagon truly has the potential to change the narrative for disordered targets."

About Ambagon Therapeutics

Ambagon Therapeutics is a biotechnology company pioneering methods to unlock intrinsically disordered protein targets using small molecules. Ambagon applies deep knowledge of 14-3-3 proteins and a proprietary suite of drug discovery tools to create molecular glues that stabilize 14-3-3:target complexes. These molecular glue stabilizers amplify native biology to restore or inhibit target function, potentiate target activity, or promote or block target degradation.
Ambagon's initial focus is on oncology, with five programs in discovery. It has locations in San Carlos, California, and Eindhoven, the Netherlands.

About 14-3-3 Biology

Ambagon's platform harnesses the biology of the regulatory hub protein 14-3-3, which reads serine/threonine phosphorylation. With more than 3000 client proteins reported, 14-3-3 has a vast interactome, enabling the manipulation of a broad range of biology across indications.

In binding its clients, 14-3-3 imposes order on disordered client protein sequences, conferring druggability on otherwise undruggable proteins and protein regions.

About the Modular Ambagon Drug Discovery Platform

By selectively stabilizing the interaction between 14-3-3 and a 14-3-3 client protein, Ambagon can create first-in-class drugs addressing high value targets inaccessible by other means, particularly those with a high degree of disorder, including transcription factors, adaptor/scaffolding proteins, and RNA binding proteins.

Because of the way that 14-3-3 interacts with its clients, Ambagon can also manipulate the biology of targets that are otherwise druggable in orthogonal ways, allowing for the development of best-in-class molecules.

Ambagon's projects begin with an x-ray crystal structure of a binary 14-3-3:target complex to inform chemical starting points from Ambagon's proprietary chemical library, conferring a high degree of

modularity to the platform. Drug discovery efforts are subsequently driven by both high throughput x-ray crystallography characterizing ternary 14-3-3:target:compound complexes and proprietary functional readouts elucidating the biological consequences of stabilization.

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