City Therapeutics Launches with $135 Million Series A Financing to Lead the Future of RNAi-based Medicine

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Harnessing next-generation siRNA engineering to improve and expand the therapeutic reach of RNAi-based medicines

Building sustainable product engine for innovative RNAi therapeutics to make a significant impact for patients across multiple disease indications, with first program expected to enter clinical development at or around year-end 2025

Led by founding Alnylam CEO and RNAi therapeutics pioneer John Maraganore, Ph.D., as executive chair and co-founded by key scientists and business leaders in RNAi

CAMBRIDGE, MA, October 8, 2024 – City Therapeutics, Inc. announced its launch today with a vision to lead the future of RNA interference (RNAi)-based medicine. City Therapeutics™ aims to harness next-generation engineering of small interfering RNAs (siRNAs) – the "trigger" molecules that mediate RNAi –to build a robust and sustainable product engine and expand the therapeutic reach of RNAi-based medicines. Led by executive chair John Maraganore, Ph.D., founding CEO of Alnylam Pharmaceuticals, Inc., the company has completed a $135 million Series A financing led by ARCH Venture Partners, with participation from other leading life sciences investors including Fidelity Management & Research Company, Invus, Slate Path Capital, Rock Springs Capital, Regeneron Ventures, AN Ventures and other undisclosed investors.

"At Alnylam, we launched the birth of RNAi therapeutics as a new class of medicines, making a profound difference in the lives of patients with unmet needs. We see the potential for RNAi to emerge as the next major category of high-impact medicines, rivaling if not exceeding the success of monoclonal antibodies. New innovation is needed to realize this future, and we believe City Therapeutics can lead this next chapter," said John Maraganore, Ph.D., co-founder and executive chair of City Therapeutics. "To unlock the full potential of RNAi-based medicines, we will utilize next-generation engineering technologies to advance innovations in siRNA design, delivery and targeting that enable improved potency and specificity, broader access across more tissue types, and expanded opportunities in multiple therapeutic areas. We are excited to launch City Therapeutics to lead the future of RNAi-based medicines."

Unlocking the next wave of RNAi-based medicines

City Therapeutics is building an siRNA-engineering platform aimed at designing, improving and optimizing RNAi-based medicines. Certain platform pillars include:

- The design of novel RNAi triggers, including those with smaller size, novel cellular mechanisms and improved potency, efficiency and specificity. Examples include cleavage-inducing tiny (city) RNAs that induce target mRNA cleavage through distinct proteins to silence gene expression.
- Purposely tailored targeting ligands for specific and enhanced delivery of engineered siRNAs to a broader range of cells and tissue types.
- Leveraging the latest advancements and insights in human genetics to address both novel and validated therapeutic targets and optimize clinical development.

City Therapeutics is building a pipeline of innovative RNAi therapeutics, with its lead program expected to enter clinical development at or around the end of 2025. Thereafter, the company's product engine is aimed at delivering a sustainable flow of high impact RNAi-based medicines, with one to two new Investigational New Drug applications (INDs) per year starting in 2026.

"Recent scientific advancements and technologies have opened the door to novel and improved engineering of RNAi trigger molecules, allowing this highly specific class of medicines to be better optimized and address more diseases. These serve as the foundation for the City Therapeutics platform and our opportunity to lead the next generation of RNAi therapeutics," said Tracy Zimmermann, Ph.D., chief scientific officer of City Therapeutics. "As we continue to build our platform, we are executing on a fast-to-clinic strategy to drive sustainable pipeline growth, with the goal of generating one to two INDs per year. With our first RNAi program rapidly advancing toward the clinic, we believe we are well-positioned to make a significant impact for patients across multiple disease indications, helping shape the future of RNAi."

Co-founded and led by pioneers in RNAi

City Therapeutics is led by many of the creators of the first generation of RNAi therapeutics. Management team and board members include:

- Barry Greene, board member; CEO of Sage Therapeutics and former President of Alnylam Pharmaceuticals
- John Maraganore, Ph.D., co-founder and executive chairman; former/founding CEO of Alnylam Pharmaceuticals
- Robert Nelsen, co-founder and board member; managing director and co-founder of ARCH Venture Partners
- Ari Nowacek, M.D., Ph.D., co-founder and SVP, corporate development; partner at ARCH Venture Partners
- Ron Philip, board member; CEO of Orbital Therapeutics and former CEO of Spark Therapeutics
- Sebastian Trousil, Ph.D., co-founder and chief operating officer; formerly at RTW Investments
- Tracy Zimmermann, Ph.D., CSO; former chief development officer of Generation Bio and former senior director, research at Alnylam Pharmaceuticals

Additional co-founders and advisors include:

- Mark Keating, M.D., co-founder; former lead scientist at Alnylam Pharmaceuticals
- Kotaro Nakanishi, Ph.D., co-founder; professor of biochemistry at The Ohio State University
- Yukihide Tomari, Ph.D., co-founder; professor in the Institute of Molecular and Cellular Biosciences at The University of Tokyo
- Hans-Peter Vornlocher, Ph.D., scientific advisor; senior advisor to Axolabs
- Phillip D. Zamore, Ph.D., co-founder; chair and professor, RNA Therapeutics Institute of UMass Chan Medical School and investigator, Howard Hughes Medical Institute; former co-founder of Alnylam Pharmaceuticals

“As an early investor in Alnylam, ARCH supported the creation of RNAi medicines as a new frontier of medicine. The time to re-enter the RNAi revolution is now, and our investment in City Therapeutics is based on our conviction that RNAi therapeutics will expand as a major category of breakthrough medicines,” said Robert Nelsen, founding board member of City Therapeutics and managing director and co-founder of ARCH Venture Partners. “City’s experienced team, leading scientific founders and versatility of its engineering platform combine to create an enormous opportunity and offer an excellent foundation to build the industry’s next leading RNAi company.”

About City Therapeutics

City Therapeutics is a biopharmaceutical company harnessing next-generation engineering of small interfering RNAs (siRNAs) to improve and expand the reach of RNAi-based medicines. The company is building a pipeline of innovative RNAi therapeutics to make a significant impact for patients across multiple therapeutic areas. Co-founded by pioneering executives and scientists in RNAi, City Therapeutics is based in Cambridge, MA, and has raised $135 million from leading life sciences investors. For more information, please visit us at www.citytx.com and follow us on LinkedIn.

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