Septerna Launches with $100 Million Series A Financing to Expand the Frontier of GPCR-targeted Medicines using the Native Complex™ Platform

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Septerna's proprietary technology recapitulates GPCRs with their native structure, function and dynamics for unprecedented drug discovery for many diseases

Founded by preeminent scientific leaders in the biology and structure of G protein-coupled receptors (GPCRs)

Financing led by Third Rock Ventures with significant support from world-class group of investors

SOUTH SAN FRANCISCO, Calif. – January 27, 2022 – Septerna, Inc., a biotechnology company discovering and advancing novel small molecule medicines targeting G protein-coupled receptors (GPCRs), today announced its launch and Series A financing of $100 million. The Series A financing was led by Third Rock Ventures with significant support by Samsara BioCapital, BVF Partners, Invus Financial Advisors, Catalio Capital Management, Casdin Capital and Logos Capital. Septerna's proprietary Native Complex™ Platform recapitulates GPCRs with their native structure, function, and dynamics outside of the cellular environment which enables industrial-scale drug discovery using novel screening technologies and structure-based drug design for the first time. Septerna is using the Native ComplexTM to overcome historic challenges of reaching the vast untapped potential of GPCR drug targets for a wide range of diseases.

"GPCRs have proven to be the most prolific class of drug targets to date, representing approximately one-third of all approved drugs and extending across all major disease areas. However, the complexity and transmembrane nature of GPCRs have made them difficult to isolate outside of the cell and inaccessible to modern small molecule drug discovery approaches," said Robert Lefkowitz, MD, co-founder of Septerna and professor of medicine, biochemistry, and chemistry at Duke University and Nobel laureate for his discovery of the inner workings of GPCRs. "Septerna's truly innovative approach with the Native ComplexTM ushers in a new era of drug discovery to reach previously undruggable GPCRs and enable all modern drug discovery technologies to be fully accessible for the GPCR target class."

The Series A financing will enable Septerna to advance its emerging pipeline of novel GPCR-targeted drug programs, enabled by the Native ComplexTM Platform and spanning multiple therapeutic areas. In addition, the company will continue to build its industrialized platform to enable drug discovery across the entire GPCR superfamily and to uncover novel mechanisms and new opportunities for previously difficult-to-drug GPCRs to address many diseases.

"Septerna is establishing a new future for GPCR-targeted medicines for patients. We already have strong momentum advancing our pipeline of small molecule drug discovery programs on the path to creating high-impact medicines," said Jeffrey Finer, MD, PhD, chief executive officer and co-founder of Septerna and venture partner at Third Rock Ventures. "In creating Septerna, our team of scientists and drug hunters took on the challenge of making the Native ComplexTM a reality by building an industrialized platform from the ground up, capable of controlling GPCRs in a revolutionary new way to catalyze a new era of GPCR drug discovery. Our team is bolstered by the unmatched brain trust of our scientific founders and advisors who are world-renowned innovators spanning all aspects of GPCR science and pharmacology."

World class team of drug developers and GPCR experts

"The Septerna team has made impressive progress building the GPCR Native ComplexTM Platform and creating a new paradigm for discovering GPCR-targeted medicines," said Jeffrey Tong, PhD, chairman of the board of Septerna and partner at Third Rock Ventures. "This is the right team, with the right technology, at the right time, because Septerna's innovation unlocks full access to modern drug discovery technologies – that have been applied successfully to kinases and other drug classes – to use for broad GPCR drug discovery for the very first time."

The Septerna team brings together experienced biotechnology leaders with deep expertise in company building, drug discovery and clinical advancement of novel medicines. Company leaders include Jeffrey Finer, MD, PhD, chief executive officer; Alan Ezekowitz, MD, DPhil, chief medical officer; Dodzie Sogah, PhD, chief operating officer; Uwe Klein, PhD, senior vice president biological sciences; Daniel Long, DPhil, senior vice president drug discovery; Richard Hansen, PhD, vice president technology; Christopher Heise, PhD, vice president discovery biology; Amer Mirza, PhD, vice president disease biology; Kara Halvorsen, head of human resources; and George Xu, PhD, director corporate strategy and portfolio development.

Scientific founders of Septerna have track records that span decades of groundbreaking discoveries that reveal the inner workings and molecular pharmacology of the GPCR family.

- **Robert Lefkowitz, MD,** James B. Duke Professor of Medicine and Professor of Biochemistry and Chemistry at Duke University, and an Investigator of the Howard Hughes Medical Institute. Dr. Lefkowitz is known for his groundbreaking discoveries that reveal the inner workings of GPCRs, for which he was awarded the 2012 Nobel Prize in Chemistry and

elections to both the National Academy of Sciences and the National Academy of Medicine.

- **Arthur Christopoulos, PhD,** Professor of Analytical Pharmacology, Dean of the Faculty of Pharmacy & Pharmaceutical Sciences, and Director of the Neuromedicines Discovery Centre at Monash University, Australia. Dr. Christopoulos is a world-leading expert in GPCR molecular pharmacology and made seminal discoveries of allosteric modulation of GPCRs, for which he has been elected to both the Australian Academy of Science and the Australian Academy of Health and Medical Sciences.
- **Patrick Sexton, PhD, DSc,** Professor, Drug Discovery Biology at Monash University, Australia and Director of the ARC Centre for Cryo-electron Microscopy of Membrane Proteins. Dr. Sexton is an international leader in GPCR biochemistry, pharmacology, and structural biology and his team is at the forefront of using cryo-EM to elucidate the structure and dynamics of GPCRs.

Additionally, Septerna has enlisted the support of advisors who are experts in the fields of GPCR biology, technology, and drug discovery. They include Bryan Roth, MD, PhD, Professor of Pharmacology at the University of North Carolina School of Medicine; Aashish Manglik, MD, PhD, Associate Professor, Pharmaceutical Chemistry at the University of California, San Francisco; Craig Lindsley, PhD, Professor of Pharmacology, Chemistry and Biochemistry at Vanderbilt University; and Ron Dror, PhD, Associate Professor of Computer Science and of Molecular and Cellular Physiology and Structural Biology at Stanford University.

About GPCRs
G protein-coupled receptors (GPCRs) are the largest and most diverse family of cell membrane receptors, and humans have hundreds of different GPCRs, each involved in controlling specific biological functions. GPCRs on the surface of each cell bind a wide range of external signaling molecules from throughout the body, and the GPCR transmits the signal across the cell membrane to drive internal cellular mechanisms. GPCRs have been widely studied as drug targets and are the largest family of proteins targeted by approved drug products. An estimated 700 approved drugs target GPCRs, representing approximately one-third of all currently approved drugs. Despite the pharmacological success of GPCRs as a drug class to date, the large majority of potential therapeutic GPCR targets remain undrugged.

About Septerna
Septerna, Inc., is a biotechnology company creating broad new drug discovery opportunities across many disease areas for the abundant drug target class of G protein-coupled receptors (GPCRs). The company's Native Complex™ Platform recapitulates GPCRs with their native structure, function, and dynamics outside of the cellular environment to enable new technologies for industrial-scale drug discovery for the entire GPCR target class for the first time. Septerna has an emerging pipeline of GPCR-targeted small molecule drug discovery programs, along with growth potential to reach many GPCRs that have been undruggable and unexploited to date. Septerna was launched in 2022 by scientific founders who have made groundbreaking GPCR discoveries and by founding investor Third Rock Ventures. For more information, please visit www.septerna.com.

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