Revolution Medicines Reports New Application of Tri-Complex Modality for “Undruggable” Protein Targets and Announces License to Ginkgo Bioworks to Explore Potential Use Against Novel Coronavirus

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Newly Discovered Natural Product and Designed Analogues Bind to Human Protein that is Exploited by the SARS-CoV-2 Virus

REDWOOD CITY, Calif. and BOSTON, June 30, 2020 (GLOBE NEWSWIRE) -- Revolution Medicines, Inc. (Nasdaq: RVMD), a clinical-stage oncology company focused on developing targeted therapies to inhibit frontier cancer targets, today announced the publication of an original scientific paper in the *Proceedings of the National Academy of Sciences.* The report describes a natural compound (WDB002) and semi-synthetic analogues that potently bind and inhibit human centrosomal protein 250 (CEP250) by forming tri-complexes with an intracellular chaperone protein. This finding represents an example of high-affinity binding to protein domains known as “coiled coils” that are notoriously refractory to conventional drug discovery approaches, and highlights the potential for this binding modality to be useful in developing drugs against difficult disease targets. Additionally, CEP250 was described by scientists at the University of California, San Francisco as an interaction partner of the Nsp13 protein of SARS-CoV-2, the virus causing the global COVID-19 pandemic. This raises the possibility that CEP250 may be a relevant disease target against COVID-19 and that WDB002 may be a useful starting point for new antiviral drug candidates.

Revolution Medicines has licensed intellectual property to Ginkgo Bioworks, the organism company, to develop WDB002 and its related compounds as possible therapeutics to treat infectious disease. Last year, Ginkgo Bioworks acquired Revolution Medicines’ genome mining platform, a technology that enables the discovery and development of novel natural product therapeutics. Ginkgo is expanding research into WDB002 and related compounds for possible applications against COVID-19.

“While Revolution Medicines remains focused on our mission of developing targeted oncology therapies using advanced approaches such as tri-complex inhibitors against frontier cancer targets, we also recognize the potential relevance of these latest research findings to the ongoing battle against COVID-19. We acted swiftly to get this intellectual property into the hands of the Ginkgo Bioworks team, which has shown a commitment to applying its broad expertise in synthetic biology to infectious disease research and development,” said Mark A. Goldsmith, M.D., Ph.D., chief executive officer and chairman of Revolution Medicines. “We believe this cooperative approach will facilitate effective partnerships with the broader scientific community to speed discoveries that may be impactful in this public health crisis and beyond.”

“We remain committed to doing our part to address the COVID-19 pandemic,” said Jason Kelly, co-founder and CEO of Ginkgo Bioworks. “Based on the early findings from this paper, we are synthesizing these compounds and screening them to validate their potential as novel antiviral therapeutics. If successful, we hope to collaborate with a pharmaceutical partner to quickly and effectively develop the drug candidate.”

The paper published in the *Proceedings of the National Academy of Sciences* is titled, “Genomic discovery of an evolutionarily programmed modality for small-molecule targeting of an intractable protein surface,” and can be accessed at: https://www.pnas.org/content/early/2020/06/29/2006560117

About WDB002 and CEP250 Binding Compounds

WDB002 was discovered by scientists at Warp Drive Bio, a subsidiary of Revolution Medicines, using proprietary genome mining technology. It is a natural compound produced by certain bacteria that binds to and inhibits the function of CEP250, a core centrosomal protein that plays a role in interphase of the cell cycle. WDB002 binds to a featureless “coiled coil” domain of CEP250 with very high affinity by forming a tri-complex that exploits the surfaces of both CEP250 and an abundant cellular chaperone protein (called FKBP12) as its ligand-binding pocket. These scientists further created modified variants of the natural product with similar CEP250 binding activity. Revolution Medicines utilizes its proprietary tri-complex technology platform to design novel targeted therapies that inhibit elusive frontier cancer targets such as oncogenic RAS(ON) proteins.

About Revolution Medicines, Inc.

Revolution Medicines is a clinical-stage oncology company focused on developing novel targeted therapies to inhibit elusive high-value frontier cancer targets within notorious growth and survival pathways, with particular emphasis on RAS and mTOR signaling pathways. The company possesses sophisticated structure-based drug discovery capabilities built upon deep chemical biology and cancer pharmacology know-how and innovative, proprietary technologies that enable the creation of small molecules tailored to unconventional binding sites.

The company’s pipeline includes RMC-4630, a clinical-stage drug candidate that is designed to selectively inhibit the activity of SHP2. Additionally, the company is developing a broad portfolio of inhibitors of other key frontier oncology targets within the notorious RAS pathway, as well as the related mTOR signaling cascade. These include inhibitors of multiple mutant RAS proteins and SOS1, as well as RMC-5552, a development candidate within the company’s 4EBP1/mTORC1 program currently in IND-enabling studies.

About Ginkgo Bioworks

Headquartered in Boston, Ginkgo Bioworks uses the most advanced technology on the planet—biology—to grow better products. The company's cel programming platform is enabling the growth of biotechnology across diverse markets, from food to fragrance to pharmaceuticals. Ginkgo is also actively supporting a number of COVID-19 response efforts, including community testing, epidemiological tracing, vaccine development and therapeutics discovery. For more information, visit www.ginkgobioworks.com.

Forward Looking Statements

This press release contains forward-looking statements within the meaning of the U.S. Private Securities Litigation Reform Act of 1995. Any statements in this press release that are not historical facts may be considered "forward-looking statements," including without limitation statements regarding Revolution Medicines' tri-complex technology, including without limitation application of this technology to oncogenic RAS proteins or proteins like CEP250, or other disease targets; WDB002 and analogues thereof, including their usefulness as a starting point for new antiviral drug candidates; the applicability of Revolution Medicines' technologies to the ongoing battle against COVID-19; and the ability to facilitate partnerships that speed discoveries that are impactful to public health. Forward-looking statements are typically, but not always, identified by the use of words such as "may," "will," "would," "believe," "intend," "plan," "anticipate," "estimate," "expect," and other similar terminology indicating future results. Such forward-looking statements are subject to substantial risks and uncertainties that could cause our development programs, future results, performance or achievements to differ materially from those anticipated in the forward-looking statements. Such risks and uncertainties include without limitation risks and uncertainties inherent in the drug development process, including Revolution Medicines' programs' early stage of development, the process of designing and conducting preclinical and clinical trials, the regulatory approval processes, the timing of regulatory filings, the challenges associated with manufacturing drug products, Revolution Medicines' ability to successfully establish, protect and defend its intellectual property, other matters that could affect the sufficiency of Revolution Medicines' capital resources to fund operations, reliance on third parties for manufacturing and development efforts, changes in the competitive landscape and the effects on our business of the worldwide COVID-19 pandemic. For a further description of the risks and uncertainties that could cause actual results to differ from those anticipated in these forward-looking statements, as well as risks relating to the business of Revolution Medicines in general, see Revolution Medicines' Annual Report on Form 10-Q filed with the Securities and Exchange Commission on May 14, 2020, and its future periodic reports to be filed with the Securities and Exchange Commission (SEC). Except as required by law, Revolution Medicines undertakes no obligation to update any forward-looking statements to reflect new information, events or circumstances, or to reflect the occurrence of unanticipated events.

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