DARWIN HEALTH

# DarwinHealth Announces Scientific Collaboration with Prelude Therapeutics to Develop Novel Biomarkers for Multiple Oncology Candidates

## PRESS RELEASE

New York, NY – (October 12, 2021) – DarwinHealth, Inc. today announced a scientific research collaboration employing its **Biomarker Enrichment Strategies for Trials** (**BEST** platform) to elucidate novel biomarkers to guide translational trajectories for multiple oncology molecules being developed by Prelude Therapeutics.

Under the collaboration, DarwinHealth will use its proprietary, quantitative, systems biology-based algorithms, CLIA-approved technologies, and validated approaches focused on Master Regulator (MR) proteins and tumor checkpoints to identify novel protein-based biomarkers that will add significant precision to patient cohort selection for clinical trials to be conducted at Prelude's discretion in both hematologic and solid tumors.

"The goal of this biomarker-focused collaboration," explained Professor Andrea Califano, Clyde and Helen Wu Professor and Chair, Department of Systems Biology, Columbia University and DarwinHealth Co-founder, "is to assess and characterize overall and tumor-specific mechanisms-of-action of Prelude's pipeline molecules in an attempt to identify novel biomarkers that may align these agents with responsive patient cohorts. Additionally, the collaboration will mechanistically characterize potential therapeutic opportunities for Prelude's pipeline molecules targeting various oncogenic pathways across multiple hematologic malignancies and solid tumor subtypes, as selected by Prelude Therapeutics. The study will leverage the VIPER algorithm to characterize the activity of these diverse compounds against key Master Regulator (MR) protein modules (tumor checkpoints) necessary for subtype-specific tumor viability."

"The BEST initiative will provide precise and actionable compound- and tumor - specific information for assessing the potential of Prelude's pipeline molecules to invert subtype-specific tumor checkpoint activity," explained Dr. Mariano Alvarez, Chief Scientific Officer of DarwinHealth. "The purpose of such studies is to generate a range of validated compound/tumor subtype/biomarker alignments that represent evidence- and mechanism-based roadmaps for biomarker development and patient selection to potentially accelerate clinical studies."

As part of the BEST initiative, DarwinHealth will provide a comprehensive readout of the potential clinical value of select Prelude pipeline molecules across a spectrum of tumor types. Through quantitative modeling and biomarker-centric translational pathways, DarwinHealth will also assist in the design of *in vivo* validation studies to leverage key opportunities that may not be apparent using conventional technologies.

"The BEST collaboration addresses one of the critical unmet needs of the biotechnology and biopharmaceutical spaces focused on cancer drug discovery—that is, developing biomarkers highly predictive of clinical response to compounds whose ultimate effectiveness may be the result of an incompletely decipherable range of both on- and off-target drug effects directed at multiple targets of regulatory programs underlying cancer dependencies," noted Dr. Gideon Bosker, CEO and DarwinHealth Co-founder. "These uncertainties lend themselves to extending the biomarker concept beyond a drug's primary (i.e., high-affinity) target, to multi-protein classifiers identified by our integrative computational and experimental methodologies."

Notably, novel, multi-protein classifiers identified by the BEST platform have been previously reported by DarwinHealth for Multiple Myeloma (N Engl J Med 2019;381:727-38. https://www.nejm.org/doi/full/10.1056/NEJMoa1903455 ) and DLBCL (British Journal of Haematology; 02 August 2021, https://doi.org/10.1111/bjh.17730).

These technologies are ideally suited for identifying mechanistic alignments between drug candidates and cancer patients based on the ability of drugs to inactivate the patient-specific MR proteins that are necessary for tumor state maintenance. Importantly, these discoveries can be quickly matured to precision, biomarker-driven clinical human testing and commercial development.

**About DarwinHealth, Inc.**

DarwinHealth: Precision Therapeutics for Cancer Medicine is a "frontiers of cancer," technology-focused company, co-founded by CEO Gideon Bosker, MD, and Professor Andrea Califano, Clyde and Helen Wu Professor of Chemical Systems Biology and Chair, Department of Systems Biology at Columbia University. The company's technology was developed by the Califano lab over the past 14 years and is exclusively licensed from Columbia University. DarwinHealth technology has been developed to identify actionable, and frequently unanticipated mechanistic and biomarker-directed alignments at the proteomic level between small molecules and specific tumor subtypes/patient cohorts and, therefore, it positioned to accelerate development of oncology pipelines, both for small molecule and immuno-oncology-based developmental pathways.

DarwinHealth utilizes proprietary, systems biology algorithms to match virtually every cancer patient with the drugs and drug combinations that are most likely to produce a successful treatment outcome. "Conversely, these same algorithms also can prioritize investigational drugs and compound combinations of unknown potential against a full spectrum of human malignancies, as well as novel cancer targets," explained Dr. Bosker, "which make them invaluable for pharmaceutical companies seeking to both optimize their compound pipelines and discover mechanistically actionable, novel cancer targets and compound-tumor alignments."

DarwinHealth's mission statement is to deploy novel technologies rooted in systems biology to improve clinical outcomes of cancer treatment. Its core technology, the VIPER algorithm, can identify tightly knit modules of master regulator proteins that represent a new class of actionable therapeutic targets in cancer. The methodology is applied along two complementary axes: First, DarwinHealth's technologies support the systematic identification and validation of druggable targets at a more foundational, deep state of the cancer cell's regulatory logic so we and our scientific partners can exploit next generation actionability based on fundamental and more universal tumor dependencies and mechanisms. Second, from a drug development and discovery perspective, the same technologies capable of identifying potentially druggable novel targets based on master regulators, and upstream modulators of those targets. This is where the DarwinHealth oncotectural approach, with its emphasis on elucidating and targeting tumor checkpoints, provides its most important solutions and repositioning roadmaps for advancing precision-focused cancer drug discovery and therapeutics.

The proprietary, precision medicine-based methods employed by DarwinHealth are supported by a deep body of scientific literature authored by its scientific leadership, including DarwinHealth CSO, Mariano Alvarez, PhD, who co-developed the company's critical computational infrastructure. These proprietary strategies

leverage the ability to reverse-engineer and analyze the genome-wide regulatory and signaling logic of the cancer cell, by integrating data from *in silico*, *in vitro*, and *in vivo* assays. This provides a fully integrated drug characterization and discovery platform designed to elucidate, accelerate, and validate precise developmental trajectories for pharmaceutical assets, so their full clinical and commercial potential can be realized. For more information, please visit: www.DarwinHealth.com.

SOURCE: DarwinHealth

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**About Prelude Therapeutics**

Prelude Therapeutics is a clinical-stage precision oncology company developing innovative drug candidates targeting critical cancer cell pathways. The Company's lead product candidates are designed to be oral, potent, and selective inhibitors of PRMT5. Prelude's first clinical candidate, PRT543, is in Phase 1 development for advanced solid tumors and select myeloid malignancies. Prelude is also advancing PRT811, a second PRMT5 inhibitor optimized for high brain exposure, in a Phase 1 clinical trial including glioblastoma multiforme (GBM). The Company's pipeline also includes its third clinical candidate, PRT1419, an orally available MCL1 inhibitor in Phase 1 development for patients with relapsed/refractory hematologic malignancies, and its two most advanced preclinical candidates, PRT2527, a CDK9 inhibitor, and PRT-SCA2, a SMARCA2 protein degrader.

**Prelude Therapeutics Cautionary Note Regarding Forward-Looking Statements**

This press release contains forward-looking statements within the meaning of the "safe harbor" provisions of the Private Securities Litigation Reform Act of 1995, including, but not limited to, anticipated discovery, preclinical and clinical development activities, timing of availability and announcements of clinical results, the timing of the expansion portion for its Phase 1 clinical trial for PRT543 and PRT811, the timing of IND-related activities for PRT2527 and the potential benefits of the Company's product candidates and platform. All statements other than statements of historical fact are statements that could be deemed forward-looking statements. Although the Company believes that the expectations reflected in such forward-looking statements are reasonable, the Company cannot guarantee future events, results, actions, levels of activity, performance or achievements, and the

timing and results of biotechnology development and potential regulatory approval is inherently uncertain. Forward-looking statements are subject to risks and uncertainties that may cause the Company's actual activities or results to differ significantly from those expressed in any forward-looking statement, including risks and uncertainties related to the Company's ability to advance its product candidates, the receipt and timing of potential regulatory designations, approvals and commercialization of product candidates, the impact of the COVID-19 pandemic on the Company's business, clinical trial sites, supply chain and manufacturing facilities, the Company's ability to maintain and recognize the benefits of certain designations received by product candidates, the timing and results of preclinical and clinical trials, the Company's ability to fund development activities and achieve development goals, the Company's ability to protect intellectual property, and other risks and uncertainties described under the heading "Risk Factors" in documents the Company files from time to time with the Securities and Exchange Commission. These forward-looking statements speak only as of the date of this press release, and the Company undertakes no obligation to revise or update any forward-looking statements to reflect events or circumstances after the date hereof.