Category

Best Startup

Product/Solution Name

(1) DarwinOncoDiscovery, comprising the Compound-2-Clinic (C2C) Drug Discovery and Novel Cancer Targets Pipelines[1]; (2) DarwinOncoTarget and DarwinOncoTreat[2-4], NY/CA Dept. of Health approved molecular diagnostic tests for the identification of investigational and approved oncology drugs that, by inverting the activity of Master Regulator (MR) proteins representing mechanistic determinants of cancer cell states in both solid and hematologic malignancies[5], identifies precise alignments between small molecule-based therapies in patients with afflicted with a broad range of advanced malignancies[3,5,10], and; (3) Targeting the Microenvironment in Immune Checkpoint Resistance and Outcomes (T-MICRO platform), for the identification of small molecule agents able to reprogram tumor microenvironment cells, abrogating their immune suppressive phenotype[11].

Date of Approval

2019-09-13

Indications

All aggressive/metastatic adult and pediatric tumors, including both solid and hematologic malignancies, as well as orphan and rare tumors that are refractory to and/or progress on standard-of-care pharmacotherapy or radiation therapy.

Therapeutic Categories

Cancer/Oncology and Immuno-Oncology

Attached Files:

- DarwinHealth Videographic Journey.pdf

Background information and need for solution/product

With cancer care projected to cost $25.2 trillion between 2020 and 2050, with $5.3 trillion in U.S. expenditures alone[6], it has become increasingly problematic to bet on empirical cancer therapies that produce marginal increases in lifespan. Targeted and immune checkpoint therapies have been proposed as potential solutions to this challenge, yet only a minority of cancer patients (6%–25%) harbors actionable mutations or responds to immunotherapy. More critically, overall relapse and ultimate failure rates are unacceptably high, even in patients who initially respond. Therefore, more innovative, mechanism-based strategies, leveraging both computational and experimental methodologies to illuminate novel molecular targets and targeted inhibitors' polypharmacology are desperately needed.

DarwinHealth has leveraged frontiers-of-science and network-based methodologies—published in the highest impact factor journals (see 2,7-12 for instance)—to discover Master Regulator (MR) proteins representing a new class of highly conserved cancer targets and biomarkers[13]. Moreover, DarwinHealth has confirmed that drugs precisely targeting these this MR-based molecular architecture abrogate tumor viability in both preclinical and clinical studies[5,10], across a broad range of cancers[4,14]. These approaches have been reviewed in scientific journals such as Science[15] and

Nature[16], as well as in the general media.[17,18]
DarwinHealth's products and technologies now undergird numerous, large-scale co-discovery efforts with pharmaceutical and biotech companies aimed at implementing more effective and efficient drug discovery efforts via the DarwinOncoDiscovery platform1. This core drug discovery and molecular diagnosis pipeline accurately and specifically assesses drug responsiveness of individual patients[5,10]—even at the single-cell level[11]—to MR-targeting drugs that suppress tumor viability by disrupting its transcriptional identity. In summary, DarwinHealth brings published, patented, and validated scientific discoveries at the pioneering edge of cancer research to identify novel targets, ideally responsive patient cohorts, and effective oncology drugs across a broad spectrum of cancers, including agents that synergize with and have the potential to rescue immune checkpoint therapies[10].

Attached Files:

- WSJ_DarwinHealth_Cracking Cancers Code.pdf
- PRIX_GENOME WEB_DH_2.pdf

History of the development of the solution/product

DarwinOncoDiscovery—DarwinHealth's oncotecture-based platform for drug/target discovery and patient-centric molecular diagnostics—is based on four foundational, extensively validated patented technologies, collectively cited >10,000 times: (1) ARACNe[19-21], to reverse engineer cell context-specific molecular networks ; (2) VIPER[22,23], to assess protein activity from the expression of their tissue-specific transcriptional targets (including in single cells[11,12]), a critical step in MR protein discovery and drug mechanism-of-action elucidation[24]; (3) PLATE-Seq[25], a microfluidic technology for the high-throughput, low-cost generation of gene expression profiles from drug-perturbed cells ; and (4) DarwinOncoTarget[4,5]/DarwinOncoTreat[2,5,10], to predict small molecule inhibitors that invert the activity of individual MRs or the full MR repertoire.
These technologies—exclusively licensed to DarwinHealth for commercial use, where they have undergone significant development, evolution, and refinement—were developed by DarwinHealth co-founder Dr. Andrea Califano and CSO Mariano Alvarez. They represent the most extensively validated and cited suite of network-based algorithms for translational and clinical research. By combining them into a confluent cancer drug discovery platform, DarwinOncoDiscovery identifies both novel conserved targets eliciting tumor-specific essentiality and the drugs modulating their activity. More specifically, extensive literature shows that drugs that invert MR activity effectively abrogate tumor viability in vivo[2,5,10,26-28], including in cancer patients[4,5,14]; and, that MRs provide accurate clinical biomarkers of drug sensitivity[29-32]. Our scientists have recently shown these methodologies can be used to target individual transformed[33,34] or tumor microenvironment (TME)-related[11] subpopulations. permitting identification of drugs synergizing with immune checkpoint inhibitors[10], paving the road to combination therapies.
By integrating these technologies, DarwinOncoDiscovery represents a unique platform for: (a) establishing co-development partnerships to evaluate compound libraries' potential against tumor or TME cells (PMP and Compound-2-Clinic programs[1]), (b) elucidating mechanism-based biomarkers of drug response (DarwinOncoMarker and Biomarker Enrichment Strategy for Trials programs[4,29,30,32]), and (c) assessing drug sensitivity in individual patients (DarwinOncoTarget/DarwinOncoTreat NY/CA Dept. of Health approved molecular diagnostic tests[3,5,10]).

Attached Files:

- DarwinHealth Supplemental Resources.pdf

- SupportletterRustgi.pdf
- Supportletter2.pdf
- Supportletter3.pdf
- Supportletter4.pdf
- Supportletter5.pdf

Why this solution/product is innovative, the broad implications for future research, and/or how it will improve the human condition

DarwinHealth has developed the only CLIA-compliant technologies/tests for: (a) identifying molecular mechanisms controlling the transcriptional identity of normal and tumor cells; and, (b) inferring the ability of small molecule-based therapy to abrogate tumor viability with >90% accuracy[5]. These innovations have been deployed in multiple partnerships with global biopharmaceutical companies to assess the capacity of their assets to directly target tumor checkpoints in prioritized cancer subtypes[38-44]. Moreover, this work has appeared in high impact-factor publications focusing on prioritization of drugs for highly aggressive and/or rare tumors ranging from metastatic gastroenteropancreatic neuroendocrine tumors[2], gastrointestinal sarcoma[5], Wilms and rhabdoid tumors[14], and aggressive drug-resistant leukemias[35], to metastatic pancreas[5,36], breast[4,26,27,37], colon[5], and prostate adenocarcinoma, to neuroblastoma[9], meningioma[5], and GBM[7]. It has also been used to identify MRs controlling TRegs to identify small molecules synergizing with immune checkpoint inhibitors[10].
Although still only in its start-up phase, DarwinHealth and its proprietary technologies/products are improving the human condition at the front lines of cancer treatment by: (a) making cancer treatment at the patient-centric, point-of-care intersection more effective and precise, and; (b) dramatically accelerating drug discovery, while decreasing drug development and treatment costs. They address these unmet needs by identifying MRs as novel, mechanism-based cancer targets, thereby providing straightforward approaches to prioritizing drug candidates for further development. Second, by identifying mechanism-based biomarkers at the MR level, DarwinHealth improves precision of clinical research by enrolling patients who are most likely to benefit, thus decreasing costs and increasing the likelihood of positive clinical trials. Finally, by matching patients suffering from poorly responsive malignancies with those drugs targeting the molecular dependencies of their specific tumors—on a patient-by-patient basis—DarwinOncoTarget and DarwinOncoTreat address the urgent, unmet need to advance from empirical deployment of marginal therapies, especially in refractory cases, to more effective drugs shown, through MR targeting facilitated by DarwinHealth technologies, to produce more enduring clinical outcomes.

Attached Files:

- Cancerpubtrials.pdf

Please provide appropriate references (ie Pubmed links)

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- DarwinHealth Supplemental Referencesupdated.pdf