Category

Best Startup

Product/Solution Name

Cellarity Platform

Date of Approval

N/A

Indications

n/a

Therapeutic Categories

multiple

Attached Files:

- PrixGalien Application 2023 530.docx

Background information and need for solution/product

Early in the drug discovery process, a big bet is placed on developing a drug against a single target, even though the underlying molecular pathology for many chronic diseases, which are the leading cause of disability and health care costs in the US, is poorly understood. Many of these complex diseases are not driven by a single target or genetic driver and have therefore defied our current drug discovery paradigm.

This current drug discovery approach was designed to address simple descriptions of biology based largely on technologies that are now more than 3 decades old. While this approach has generated several very successful therapies, it is highly inefficient as ~$83 billon is being spent on RD annually while only 1 in 10 drugs make it to patients and thousands of diseases go without treatments.

Unsatisfied with the lack of predictiveness and excessive clinical failure rate of this process, we developed the Cellarity Platform with the mission to fundamentally redesign the way drugs are created.

The purpose of the Cellarity Platform is to discover novel small molecules that target the underlying cellular dysfunction of disease, instead of a single molecular target.

The platform is an entirely new approach to drug discovery. Focusing on the cell allows us to see biological systems in full, and not through the proxy of a single target. The AI models within the platform utilize data at single cell resolution to identify cell state transitions that drive disease and to identify compounds that can revert these disease state transitions. This approach uncovers novel actionable biology, even in diseases with no known targets, and designs non-intuitive chemistry. Most importantly, because the cell is a much fuller representation of disease, the Cellarity platform is designed to drive much higher clinical success.

Attached Files:

- Cellarity Overview .pptx

History of the development of the solution/product

Cellarity was founded by Flagship Pioneering in 2017 to fundamentally redesign the way drugs are created and to do this, we couldn't change just one aspect of drug discovery. We had to change the whole paradigm.

We don't often know the underlying molecular pathology of complex diseases, which are a major challenge for drug discovery with growing unmet clinical needs. The industry is currently trying to address these diseases by making more and more selective drugs—small and large molecules targeting just one particular protein in the body. Changing the paradigm of drug discovery starts with moving from a target-centric approach to completely focusing on the cell. This allows us to look for more and see more of the biology of complex diseases, and if we are able to do that, we can create better medicines and do more for more patients.

With that in mind, Cellarity's journey began with the recognition that powerful new biological and computational technologies exist to perturb and quantify virtually any cellular or molecular component. The vision was that these technologies could generate the data necessary to unravel biological complexity with the aspiration to produce drug candidates with improved translatability throughout the discovery and development process.

Thus, Cellarity was created—a first-of-its-kind therapeutics company—to develop medicines by studying and altering the cellular signatures of disease. With the unique ability to create drugs through the lens of the entire cell, Cellarity strives to increase the success of drug discovery and address the presently intractable diseases for which casual targets are either undruggable or unknown.

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

Cellarity has developed a broad platform harnessing single-cell technologies and machine learning to unveil the network state of a given cell, defining the cell's behavior. Because Cellarity solves for a functional readout combined with a cell behavior change, and not a proxy like traditional drug discovery does by modulating a particular target, we can uncover previously undiscovered mechanisms of disease and complex behavior of cells that would not have been discovered with a traditional target-centric approach. This allows us to look for more and see more of disease biology and ultimately create more effective medicines and do more for more patients.
In recent years, we've seen major advances in high resolution data, single-cell technologies, and AI/ML. Cellarity's platform digitizes and quantifies cellular behaviors, unravels the network dynamics that govern those behaviors, and generates medicines that can direct them. By computationally understanding the changes that occur within a cell that make it transition from health to disease, we can design novel therapies that yield a desired set of changes, going beyond a single target, and instead broadly addressing cellular behavior that is driving disease.
Cellarity's cell-first paradigm is an entirely new approach, and we believe Cellarity is the only company today that combines high-resolution data, single cell technologies, and ML to encode biology, simulate interventions, and purposefully design breakthrough medicines. To do this, we first identify the set of cellular changes that underlie the start and progression of a disease. AI lets us model computationally

the changes that occur in these systems when they move between health and disease, and it can also model the actions of various pharmacologic interventions.

This approach allows us to understand and address diseases with previously undiscovered mechanisms and even complex multicellular origins. Furthermore, by focusing on the cellular changes that underlie disease instead of a single target, Cellarity's approach uncovers new biology and treatments and is scalable and applicable to virtually any disease.

The Cellarity platform has the ability to work across any disease condition, especially complex diseases, which currently challenge the drug discovery industry. This is exemplified by Cellarity's drug discovery programs. Each program differs in complexity of cell type and behavior, and they range from diseases with a specific cellular dysfunction found in one cell type – like sickle cell disease – to diseases with multiple forms of dysfunction across multiple cell types – such as metabolic disease. Cellarity's technology also enables scale, because findings in one program can be used across subsequent programs that share tissue, cell types, or underlying cellular dysfunction.

An example of innovation we achieved with our platform technology is in our metabolic disease program. For this program, we asked the question: What if we could reprogram white fat cells, the fat cells that store fat, into beige fat cells, the fat cells that burn energy? If we did that, we could have a significant impact on several metabolic diseases.

We created a Cellarity Map, a digital analysis of cell behavior, to model the transition between white fat cells, obtained from obese individuals, to beige fat cells, obtained from lean individuals. Next we deployed our platform to design compounds that drive this transition. What we quickly discovered through our ML algorithms was multiple interventions that were predicted to drive this biology. We then took these predicted interventions and tested them, in vitro and in vivo in non-human primates and found impressive improvements in insulin sensitivity, glucose tolerance, and lipid profiles. This shows that our in-silico predictions translated into measurable biological results. We are now evaluating a path to clinical trials.

In our hematology program for sickle cell disease, we have demonstrated in preclinical studies the ability for our platform to engineer new small molecules that exceed standard of care and are equivalent to gene therapy. We began by a digital analysis of cell behaviors that increase the production of fetal hemoglobin to offset ineffective adult hemoglobin variants seen in patients. Our ML algorithms identified several compounds that in vitro drove red blood cell progenitors to a high fetal hemoglobin production. Using our platform and rich single cell data, we were also able to explain the MoA of these compounds vs those of standard of care and gene therapy, giving us high confidence in our differentiation and potential impact for patients. Finally, the abundance of data that our platform generated pointed us to a novel molecular mechanism for fetal hemoglobin induction. This mechanism has never before been associated with this biology and is attractive vs competitor small molecule fetal inducers because it works through a non-cytotoxic mechanism. With all this in hand, we are currently deploying structure-based design approaches to optimize our leads towards the clinic.

Cellarity currently has several programs underway in metabolic disease, hematology, and immunology. Our broad pipeline in multiple therapeutic areas demonstrates the scale and potential of Cellarity's platform to develop new therapies for a wide range of diseases. The goal now is to advance the first programs into the clinic.

Please provide appropriate references (ie Pubmed links)

1. https://pubmed.ncbi.nlm.nih.gov/33558698/
2. https://pubmed.ncbi.nlm.nih.gov/31363220/
3. https://pubmed.ncbi.nlm.nih.gov/30890159/
4. https://www.nature.com/articles/s41587-020-0591-3
5. https://datasets-benchmarks-proceedings.neurips.cc/paper/2021/hash/158f3069a435b314a80bdcb024f8e422-Abstract-round2.html

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