

Agenus' Artificial Intelligence (AI)

Creating our Nextgen I-O Treatments

Big Data is increasingly used for identifying trends and guiding strategy. At Agenus, we have developed a proprietary AI platform - Adaptive Learning Platform Systems (ALPS) to provide insights into cancer biology and help identify new targets for drug development. ALPS is also designed to help predict responses to treatment and with the development of precision combinations.

We take data from genetic analysis of millions of immune cells in our laboratory and from collaborators, and we match them with tumor profiles of patients from our clinical trials.

These capabilities hold the answers to some of the most important questions in cancer immunotherapy. Including, why do current immunotherapy medicines work so well in some patients but not others? What determines whether a treatment will be effective in a particular patient? Using ALPS, we are finding answers to some of these questions. In doing so, we expect to develop effective treatment strategies for wider numbers of cancer patients who are not benefiting from today's medicines.

ALPS is Intended to Help us Develop Effective Therapies for Patients

Determining a patient's "immune fitness" is key to their treatment

The state of a patient's immune system is called "immune fitness". It is determined by an individual's genetic background inherited from their parents. In addition, environmental factors such as exposure to pathogens throughout their life, also influences their immune fitness. The overall immune fitness eventually determines whether an individual's immune system can "see" dangers such as cancer cells and how strongly their immune system can be mobilized to eliminate cancer. Quantifying a patient's immune fitness along with the aggressiveness of their tumor is key to 1) understanding the cancer-killing potential of a patient's immune system and 2) determining the best treatment strategy for a potent immune response to try and kill their cancer. **All of this requires algorithms to help design, make and test the best treatments for patients with cancer. Agenus scientists are using ALPS to potentially achieve such breakthrough outcomes.**

ALPS algorithms provide vital information to help design optimal treatment strategies for patients. For example, a patient's immune fitness and the visibility of their

tumor may help with the choice between a combination of checkpoint antibodies such as Agenus' AGEN1884 and AGEN2034 or a combination of antibodies with immune-educating vaccines.

Identifying new ways to rejuvenate "tired" T cells could make the difference between life and death

Cancer fighting T cells often get tired after they kill a certain number of tumor cells. To maintain a sustained killing of cancers, these tired T cells must be "energized". Agenus scientists have leveraged the ALPS platform to analyze thousands of T cells that get exposed to cancer cells. **Based on this analysis, we have identified T cells that we believe maintain their ability for cancer cell killing.** Our proprietary algorithms that compare genetic and immunological data from these high energy T cells versus tired T cells are designed to help us identify targets that revert "tired" T cells into energized cancer-killer cells. We have also identified other targets that we believe may help sustain the fighting ability of cancer-killer T cells. Our ALPS platform has also helped us identify novel targets to guide our clinical development strategy by providing vital

information to determine which approach to take for combination treatments.

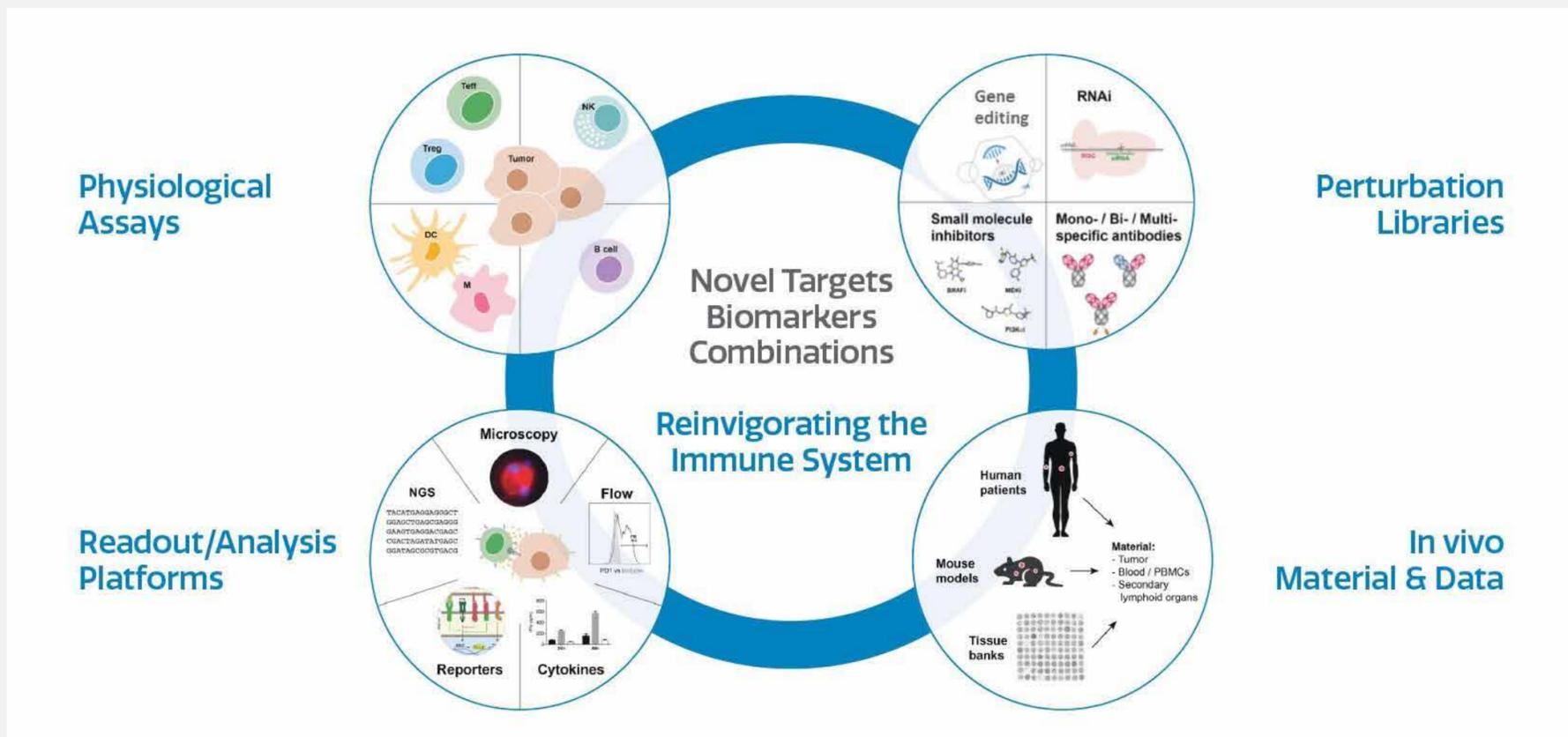
Predicting and measuring responses to immunotherapy is key to designing treatments; informing our rapid clinical development plans

Immunotherapies have led to successful and sometimes curative treatments of previously incurable cancers. However, this has been in a small subset of patients. The ability to determine which patients are going to respond to currently available treatments will have important benefits. These include the ability to target such treatments to only those likely to respond and to pursue new treatments for those who will not. Leveraging deep learning algorithms with ALPS, we have developed ways that we believe can predict the potential clinical outcomes of immune checkpoint inhibitors based on how "immunogenic" a patient's tumor is, which is an indicator of how visible the tumor is to the immune system. To accomplish this, we analyze vast datasets from internal and external databases, from our clinical trials, and our laboratory experiments. We

algorithmically analyze all this to identify new mechanisms that show how tumors escape an immune attack. The results inform our clinical combination strategy of Agenus drugs which are specifically designed to block mechanisms that interfere with immune systems' war on cancer.

Novel target discovery for next generation cancer vaccines

To develop our next generation anti-cancer vaccines, we analyze massive volumes of data, including DNA and RNA expression profiles from a patient's tumor. This helps us characterize a patient's cancer as well as his or her immune system. These data streams are fed into ALPS where a workflow of deep learning algorithms - called AIM -- identifies the unique neoantigens expressed by the tumor. This helps with the recognition of the patient's unique tumor to be recognized by the patient's own immune system. Such recognition is key to triggering an effective anti-tumor immune response. ALPS discovered neoantigen targets are then used to design a vaccine blueprint, which could be custom manufactured for that patient.



Adaptive Learning Platform Systems (ALPS)

Twenty-five years ago, Agenus started its journey on the road to cancer immunotherapy. Today, immuno-oncology is a data rich field, ripe for harvest. Agenus' ALPS platform leverages big data from tumor-genomics. ALPS also recognizes the importance of big data from the immune system (immunomics). Integrated together and analyzed with our cutting-edge AI and machine learning algorithms, ALPS is a foundational element of our elegant innovation and discovery engines.

Forward-Looking Statements: This Agenus News Brief includes forward-looking statements that are made pursuant to the safe harbor provisions of the federal securities laws, including statements regarding Agenus proprietary AI platforms and their anticipated capabilities and advantages, as well as Agenus' clinical development strategies. These statements are subject to risks and uncertainties, including those described in our SEC filings.