

## Driving Innovation with Computational I-O

Cancer is a complex disease that involves multiple molecular pathways, protein and gene interactions in a variety of different cell types. Detailed knowledge of these complex interactions is key to delivering curative treatment to patients. We believe that we can now address this challenge using Computational I-O. With this approach, we generate and analyze data from genetic studies (such as gene sequencing), to understand how genes and proteins interact in normal and disease states. This allows our researchers to assign function to specific segments of the genome. In this Newsletter, we discuss key features of our unique platform.

### Agenus' Computational I-O Platform is Designed to Deliver Curative Treatments

#### Our platform is designed to deliver next-generation I-O molecules to the clinic

Our Computational I-O platform is answering basic questions in cancer immunobiology to reveal novel therapeutic targets that could bring transformative benefits to patients. We are working to identify patients that are more likely to respond to our therapies and combinations. Coupled with Agenus' antibody discovery and engineering capabilities, deep immunobiology expertise, and fully-integrated manufacturing capabilities, our Computational I-O platform has the potential to drive the next generation of I-O therapies, including synergistic bispecific molecules.

#### Agenus' Computational I-O Platform provides new insights into the cancer fighting ability of T cells

A foundation of Agenus' Computational I-O platform is based on a human cell culture system that models interactions between T cells and tumor cells in the tumor microenvironment (TME). Our platform allows us to study this interaction over a period of two weeks. This enables us to learn how cancer-fighting effector T cells are activated, fight cancer cells and then eventually become "tired" or dysfunctional. All this data and information allows us to identify molecular signatures that correspond with the tumor cell killing capacity of T cells, as well as signatures associated with terminally dysfunctional or "tired" T cells. Agenus scientists leverage this information to discover novel drug targets and biomarkers. The ability of Agenus' Computational I-O platform to recapitulate hallmarks of intratumoral T cells power our ability to discover and optimize novel immunotherapy targets and drugs.

#### Agenus' Computational I-O Platform has key advantages

Agenus' Computational I-O is:

- **Flexible** – to interrogate multiple aspects of antitumor immunity, including T cell dysfunction, innate immune regulation, stromal interactions and other therapeutic resistance pathways
- **Longitudinal** – T cell and cancer cell interactions are monitored at many timepoints rather than at one point in time.
- **Tractable** – parallel implementation of molecular, 'omic and functional assays
- **Scalable** – high-throughput, genome-scale screening
- **Integrative** – especially powerful when combined with Agenus' end-to-end innovation and therapeutic development engines for antibodies, bispecifics and combination cell therapies

In addition to novel therapeutic development, our Computational I-O platform churns out millions of data points showing how T cells interact with tumor cells in the TME. These data points are fed into our Adaptive Learning Platform Systems ([ALPS, Issue 2, vol 5](#)) for further analysis. Populating ALPS with the deep, high quality and physiologically-relevant data from our Computational I-O platform maximizes its potential to support intelligent I-O clinical trial design.

 <p><b>Target Discovery</b></p> <p>Identify targets that address resistance pathways to current therapies</p> <ul style="list-style-type: none"> <li>✓ Cancer targets</li> <li>✓ T cell targets</li> <li>✓ Other immune cell targets</li> </ul>	 <p><b>Therapeutic Optimization</b></p> <p>Screen and optimize therapeutic candidates to achieve desired biologic function</p> <ul style="list-style-type: none"> <li>✓ Small molecules</li> <li>✓ Antibodies &amp; multi-specifics</li> <li>✓ Cellular therapies</li> </ul>	 <p><b>Intelligent Trial Design</b></p> <p>Maximize clinical benefit for emerging therapies and improve clinical success rates</p> <ul style="list-style-type: none"> <li>✓ Optimal combinations</li> <li>✓ Therapeutic sequencing</li> <li>✓ Predictive biomarkers</li> </ul>
<p><b>Integrated Discovery &amp; Development Engine</b></p> <p>Full process integration enables early hypothesis testing, parallel processing and rapid development of therapeutic candidates</p> <p><b>From target to IND in &lt; 24 months</b></p> <p><b>11 INDs filed in 3 years</b></p> <ul style="list-style-type: none"> <li>✓ Antibody discovery &amp; optimization</li> <li>✓ Multi-specific formats &amp; Fc engineering</li> <li>✓ Cell line development &amp; GMP production</li> </ul>		

### Agenus Computational I-O Platform To Drive Innovative Partnerships

Agenus' Computational I-O platform is a flexible system that is designed to enable us to discover novel therapeutic targets, optimize therapeutic candidates to achieve desired biologic function, and inform intelligent clinical trial design. In addition to utilizing this platform for our own pipeline development, we are also exploring discovery partnerships with other biopharma companies interested in leveraging this program for their own portfolio development.

**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 the potential of Agenus' Computational I-O Platform. These statements are subject to risks and uncertainties, including those described in our SEC filings.