agenusnews

Vol. 2, Issue 17 • September 30, 2019

Why is Agenus UK Crucial for the Rapid Discovery of Cancer Cures?

Agenus UK is the *centre of excellence for protein engineering and display technologies.* Built upon our culturally and scientifically diverse talent from all over the world, Agenus UK is our epicenter of deep expertise in bio-informatics, biophysics, immuno-oncology (IO) biology and immunology, as well as cell culture, cell and protein engineering and phage display. Our team has delivered novel therapeutic formats that are the foundation of our broad and unique pipeline, including our multi-specific antibody and cell therapy[1] platforms.

Our discovery platform in the UK combined with our scientific expertise culminate in the formidable force behind our industry record of delivering 13 new IO discoveries to the clinic in ~3.5yrs; and a trajectory to continue this record setting pace. Together, we have also designed the architecture of bispecific and bifunctional molecules that are designed to achieve superior biologic outcomes over existing mono or combination approaches.

New Drug Candidates are Born and Perfected at Agenus UK

Antibodies are the foot soldiers of our immune system and have shown curative benefit for patients with cancer. To create antibody therapies with the best pharmaceutical properties, diversity is important. Our product design starts with our powerful technology platforms comprising vast repertoires of immune receptors (in excess of 10 billion clones) to make monoclonal and bispecific antibodies, chimeric antigen receptors (CARs) and T cell receptors (TCRs)[1].

To start, our scientists launch multiple campaigns using our in-house antibody display platforms (phage and mammalian) to yield a robust set of antibodies, including fully human antibodies and antibodies from our newly designed and expanded Phage Display Library. Our internally designed libraries were created to remove liabilities such as undesirable amino acid residues and known sequence incompatibilities that may delay or slow discovery. By creating our own library with modifications to address these liabilities, we are creating best in class candidates designed to have significant benefit for patients with cancer.

Superior Antibody Formats for Best Therapeutic Benefit

Our deep understanding of cancer biology and molecular mechanism of IO targets continues to be vital for delivering discoveries which have exceeded those of any company in the field with regards to first or best in class potential. Not all cancer biology can be modified by one format; that is why our scientists have access to a variety of different molecular architectures. Depending on required attributes, Agenus can tailor Fc biology, simultaneously bind two or more targets or simplify manufacturing processes.

One approach to achieve superior antibody efficacy is to create bispecific molecules that simultaneously interact with two or more biological targets within the tumor environment. To achieve superior performance, tethering more than one antibody domains together can create synergies and biological advantages to enhance efficacy and patient benefit as compared to monospecific antibody combinations.

When our clinicians and biologists studied patients that were treated with validated IO therapies, including those targeting CTLA-4, they were struck by the observation of durable and even curative responses in some patients. They quickly became committed to finding a way to expand the benefit to more patients. In consultation with our antibody design experts, our team set out on a mission to interrogate the science further and develop a CTLA-4 targeting antibody designed to expand benefit to those patients who are currently unresponsive.

Our team explored an important biological driver in patients who did not respond to the first generation anti-CTLA-4 antibody, ipilimumab: a genetic polymorphism in the Fcγ-receptor, as described in a publication in *Cancer Cell* last year. Our antibody engineers in Agenus UK created a solution by changing the format of the antibody, or more specifically, engineering the Fc region of our first generation anti-CTLA-4 molecule (AGEN1884) to create a best in class molecule (AGEN1181). We believe they have delivered what we had hoped – a molecule designed to improve on the features of a first-generation CTLA-4 and further expand benefit to more patients, including the more than 40% of patients with this genetic polymorphism. AGEN1181, is now advancing in clinical trials. We have big expectations and ambitions for this molecule, in the clinic.

Similarly, our antibody engineers have developed a way of addressing important tumor escape mechanisms by creating bispecific molecules that are able to target two or more biological agents within the tumor environment. Our novel molecule, AGEN1223, preclinically achieved levels of anti-tumor activity that we believe no combination or sequence of monospecific antibodies can achieve. In short, our team has exemplified our approach to leverage the evolving science and apply cutting edge engineering innovation to deliver novel and superior drug candidates designed to cure cancers.

Our expertise and diverse capabilities – as evidenced by those at Agenus UK – are vital to developing high performing biological intervention to defeat cancer. These attributes along with our ability to control our own diverse portfolio of agents allows us to pursue our mission uncompromisingly.

Agenus UK is Continually Innovating to Achieve Excellence and Accelerate Development Timelines

Over the last three years, Agenus UK has developed an *'End-to-End'* discovery and development process in Cambridge, UK. We strive to ensure that every antibody candidate in its selected format is biologically active and can be manufactured with minimal liabilities in order to rapidly progress into the clinic. To ensure this, at various stages in the lead antibody selection process, we have developed parallel workflows to interrogate our panel of drug candidates in robust biological assays. These assays are developed from our IO expertise, and this approach allows us to more rapidly identify a highly desirable lead candidate at industry record speeds. Cell line development (CLD) is a critical first step towards antibody manufacturing and is controlled by us in-house. We have fully integrated CLD into the drug discovery process in order to expedite transfer of novel technology and beneficial Fc biology into our lead molecules for manufacture in Berkeley, our CMC facility, and consequently fast entry into the clinic.

Agenus is planning for continued future success by keeping the gas pedal down on innovation. We invest in *disruptive technology development* to continuously innovate our platforms and processes to stay ahead in the IO field.

[1] Through subsidiary AgenTus Therapeutics

Forward-Looking Statements: This Agenus Newsletter includes forward-looking statements that are made pursuant to the safe harbor provisions of the federal securities laws, including statements regarding Agenus' record setting pace of IO discoveries and the ability to engineer antibodies in rapid fashion to achieve superior outcomes. These statements are subject to risks and uncertainties, including those described in our SEC filings.