

Ablexis, LLC

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AlivaMab Discovery Services, LLC

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Ablexis and AlivaMab Discovery Services

Unparalleled success in antibody discovery and development.

Ablexis and AlivaMab Discovery Services together launch antibody drug discovery and development projects on the fastest and most de-risked path to success. Ablexis invented and licenses the AlivaMab Mouse technology, a best-in-class suite of transgenic mouse strains designed to address the many challenges across antibody drug discovery and development. AlivaMab Discovery Services (ADS) offers innovative, comprehensive solutions for antibody drug discovery, using AlivaMab Mouse to deliver human antibodies that meet functional and developability requirements in industry-leading timelines.

Ablexis's AlivaMab Mouse

AlivaMab Mouse is a trusted and validated platform for antibody drug discovery, in use by more than a dozen of the world's top pharmaceutical companies, plus additional dozens of biotechnology companies, both public and private. AlivaMab Mouse incorporates unique design features that bring greater efficiency and higher probability of success across all aspects of antibody drug discovery and development compared to other technologies. Since its first implementation in 2015 in partners' discovery processes, multiple AlivaMab antibodies have successfully entered clinical development.

AlivaMab Mouse embodies its inventors' decades of real-world experience and success in antibody drug discovery and development combined with their in-depth knowledge of genetic engineering, B cell development and molecular immunology, yielding substantial improvements over other platforms and technologies. All strains of AlivaMab Mouse make a patented part-human/part-mouse antibody composition comprising a fully-human Fab⁽²⁾ with mouse Fc and cytoplasmic domains. The mouse-sequence domains support native signaling for fast and strong primary and secondary immune responses to drive rapid antibody generation timelines. The human-sequence portions of the constant regions, which influence the activity of the variable region of the antibody, support early and predictive quantitative assessment of function and developability and then successful reformatting of the variable region, ensuring reliability of early data and shortening discovery timelines (Fig. 1).

The curated human VH, Vk and Vλ repertoires in AlivaMab Mouse increase probability of success by lowering risks in pre-clinical and clinical development, including lowering of risks of antibody–drug immunogenicity in patients. Thoughtful combinations of human and mouse coding regions and

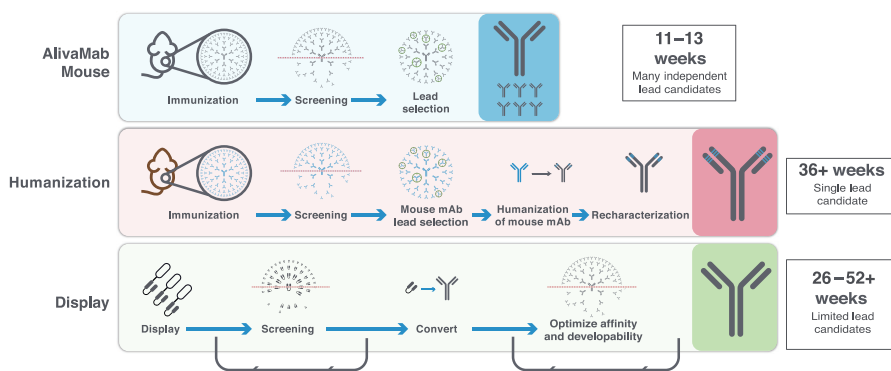


Fig. 1 | The AlivaMab Mouse platform. A trusted and validated technology for the discovery of antibodies.

cis-regulatory elements in the immunoglobulin (Ig) transgenes optimize function, for fast, diverse high-affinity IgG responses, including both TH1- and TH2-driven responses for enabling uses of different immunization strategies, and a normal, human-like expression of human Igλ light chain for greatest combinatorial diversity. The AlivaMab Ig transgenes are fully synthetic, perhaps the largest synthetic DNAs ever introduced into metazoans. The Ig transgenes are autonomously functional, which obviates the need for their insertion into the endogenous mouse immunoglobulin loci, therein avoiding hijacking endogenous mouse coding and cis-regulatory elements. This, and other careful design features, support the freedom-to-operate of AlivaMab Mouse, which should be a critical consideration when choosing a discovery platform.

AlivaMab Mouse is the most broadly adopted human therapeutic antibody discovery technology by leading pharma

Larry Green, CEO, Ablexis

"Efficiently generating candidates with very high potency, combinatorial and somatic diversity, specificity, developability and reduced chance of immunogenicity, AlivaMab Mouse is the most broadly adopted human therapeutic antibody discovery technology by leading pharma," said Larry Green, founder and Chief Executive Officer of Ablexis and founder and Executive Chairman of AlivaMab Discovery Services. "With Ablexis's flexible non-exclusive

licensing terms, dozens of companies ranging in size from pharmaceutical companies to public and private biotechnology companies have licensed AlivaMab Mouse. Over 400 projects have been conducted using AlivaMab Mouse for antibody drug discovery in various formats, from standard antibodies to formats including bispecific antibodies, antibody–drug conjugates, radio–conjugates, CARs, and immunocytokines. Ablexis continues innovating with new mouse strains in development, including strains with expanded immune responsiveness and novel formats, which are designed to continue addressing the increasing complexities of antibody drug discovery. Ablexis remains focused on supporting our partners' success in discovering and developing new antibody drugs", Green concluded.

AlivaMab Discovery Services: delivering superior antibody therapeutics

Leveraging the AlivaMab Mouse technology, ADS was founded in 2018 to be the premier partner in antibody drug discovery. "Differentiating us from others in the field, our integrated platform for discovery, developability assessment and engineering combines proven technologies and unmatched expertise to deliver superior antibody therapeutics in rapid timelines," said ADS CEO Justin Mika.

ADS is the only organization that combines the AlivaMab Mouse platform with robust discovery processes specifically designed and optimized to reliably induce strong and diverse immune responses and to efficiently recover the target-specific antibody repertoires within aggressive timelines. The company's AMMPD immunization protocols, high-throughput, customized function-first screening, suite of developability assessment capabilities, and engineering capabilities for reformatting, including bispecific

antibodies, enable ADS to successfully meet their partners' design goals, no matter the complexity. ADS accelerates timelines, improves efficiencies, and maximizes probability of success through:

- Eliciting very fast, robust, and diverse immune responses to even the most challenging targets in as little as two to six weeks, which is one to three months faster than other companies' approaches, through ADS's powerful AMMPD immunization methodologies, which include innovative protein, cell and DNA immunizations plus protocols that break immune tolerance.
- High-throughput screening of the diversity of both plasma and memory IgG⁺ B cell repertoires, interrogating up to hundreds of thousands of hybridomas, which is an order of magnitude greater than some single B cell screening technologies and even greater than other hybridoma processes.
- As early as eleven days after completion of immunization, reliable identification and ranking of up to thousands of functional hits using custom-designed functional assays that are optimized for high-throughput readouts, ensuring maximum recovery of epitope and molecular diversity in the pool of antibodies that meet functional criteria.
- Delivery of tens to hundreds of antibody lead candidates that meet design goals in just three to four months routinely, at least twice as fast as other approaches. Deliverables include recombinant fully human antibodies, sequences, and a functional, specificity, and biophysical characterization data package that includes a thorough assessment of manufacturability.

"Our immunization and screening capabilities allow identification of antibodies to targets, including rare antibody events, with exquisite functional and biophysical drug-like properties that can be missed using alternative approaches," said John "Lippy" Lippincott, Vice President of Discovery at AlivaMab Discovery Services. "Humanization and in vitro display approaches require additional steps, take longer and/or produce candidates with limited diversity and inferior development and clinical attributes. In contrast, AlivaMab Mouse naturally makes antibodies with high affinity, high potency and other drug-like qualities, and our optimized processes deliver multiple leads with diverse sequences and epitope coverage while reducing timelines. Deep screening, combined with early functional characterization ensure only the best antibodies advance," explained Lippincott.

Developability and engineering

Some of the costliest and most time-consuming obstacles in the successful transition from discovery to development are poor developability properties, such as low expression, solubility and stability, and off-target binding. To manage this risk and further reduce development time and cost to the clinic, in 2020, ADS expanded its antibody discovery services by integrating a suite of in silico and in vitro capabilities to assess developability of antibody candidates. Consequently, the company delivers diverse panels of antibody therapeutic candidates not only with extensive molecular and epitope diversities, and deep functional and kinetic characterization, but also with developability qualities required for successful antibody drug development, not only saving time and financial costs during cell-line and process development, but also de-risking clinical development.

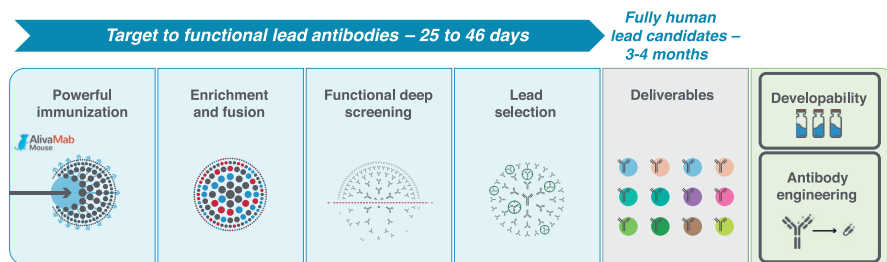


Fig. 2 | Rapid generation of antibodies. Fully human lead candidate antibodies can be discovered in just a few months.

With the recent launch of antibody engineering capabilities, ADS has further expanded its expert offerings. "Our philosophy is to start with robust and diverse raw materials (lead antibodies) from our discovery campaigns, and then to engineer and evaluate large matrices of alternative format candidate leads. This approach enables rapid identification of molecules that exhibit not only the desired activity, but are also highly expressed, highly specific, and highly stable," said Jonah Rainey, Vice President of Antibody Engineering and Protein Science. ADS delivers bispecific antibodies that are designed for valency, affinity, and geometry to drive optimal activity. Further, they are stability engineered and tested for developability to ensure drug-like properties. ADS can also provide scFvs for CARs that are specific and stable, eliminating liabilities such as off-target interactions or cell surface self-association that could lead to unwanted signaling. Engineering capabilities to modulate effector function and half-life are also available. Finally, while unnecessary to date in the discovery platform, engineering to modulate affinity and remove identifying developability risks can also be performed.

Through our unique combination of technologies, an exceptionally experienced team and flexible partnership, we maximize efficiencies and de-risk downstream development

Justin Mika, CEO,
AlivaMab Discovery Services

Leveraging scientific creativity and experience

What further sets ADS apart is its team, whose expertise and passion for science are built on decades of experience in using antibody drug discovery platforms and processes across diverse therapeutic areas, including oncology, autoimmunity, inflammatory disease, metabolic, ocular, and infectious disease. Through their collective careers in pharma and biotech, the team has conducted hundreds of antibody drug discovery projects.

As a result, whatever the requirement—developing novel functional assays, generating quality therapeutic leads on a rapid timeline, producing diverse antibodies against membrane multi-spanning targets, or breaking immune tolerance to generate highly potent, species cross-reactive antibodies—ADS will design a customized workflow to maximize diversity and speed, generating antibody candidates that meet partner-defined program requirements (Fig. 2).

"Every antibody drug discovery project is unique. Using our broad and deep expertise in the science of antibody drug discovery and its processes, including immunization, antibody recovery, antibody screening, and functional assay development and execution, the ADS team creates a tailored discovery plan to navigate around potential pitfalls and, when challenges do arise (because biology is complex), devise creative solutions to deliver large panels of target-specific, functional antibodies for the selection of antibody lead and backups for even the most challenging target product profiles," said Mika.

Partnering

The ADS business model is focused exclusively on partnership via flexible business models. There are no internal product pipelines or affiliated therapeutic discovery companies that create conflicts of interest. That is why, along with a focus on experience, communication and collaboration, ADS is trusted by top-tier pharmaceutical and biotechnology companies wanting to enhance their existing capabilities.

ADS's integrated platform is a marked improvement on other antibody discovery platforms, spanning from the collaborative process of designing the discovery plan to the rapid delivery of fully human therapeutic antibodies or engineered alternative formats, with every step of the workflow designed to create value by saving time and facilitating successful drug development. "Through our unique combination of technologies, an exceptionally experienced team and flexible partnership, we maximize efficiencies and de-risk downstream development by delivering a panel of diverse drug-quality lead candidates," said Mika. "Through this, we support our partners in bringing better medicines to patients faster."

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