

Sorrento Therapeutics, Inc.

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Unleashing the therapeutic potential of naïve human antibodies

Sorrento Therapeutics, Inc. is developing a pipeline of fully human immunotherapies selected from its proprietary G-MAB library. Backed by a platform covering discovery, advanced clinical development, manufacturing and a proven track record of commercialization, it seeks to deliver life-changing therapies.

Sorrento Therapeutics, Inc. (*Nasdaq:SRNE*) together with its subsidiaries (collectively 'Sorrento' or the 'company') is a clinical stage and commercial biopharmaceutical company developing new antibody-based oncology, anti-infective, and pain therapeutic drug candidates. Sorrento was founded on the development of passive immunization strategies, an approach that has changed the medical practice over the past two decades by allowing the rapid targeting of pathogenic antigens of exogenous, internal (self-antigens) or tumor origin. The key to developing such therapies is access to the broadest possible repertoire of human antibodies to rapidly screen them for binders to the pathogenic antigens of interest.

Sorrento's recombinant antibody phage display library, G-MAB, contains the antibody variable domains from nearly 600 donors of different ethnicity and sex, which translates into a total of more than 10 quadrillion (10^{16}) distinct antibody sequences and makes it one of the largest libraries of naïve human antibodies available in the world. These fully human antibody fragments provide the building material to construct fully human antibodies for use in immunocellular therapies, antibody-drug conjugates (ADCs), oncolytic viruses and antiviral therapies including those against coronaviruses (Fig. 1).

The company's lead programs in cancer include CD38-targeting chimeric antigen receptor T cells (CAR T) and dimeric antigen receptor T cells (DAR T) therapies in multiple myeloma, and CD38-targeting ADCs in amyloidosis. Sorrento has also harnessed G-MAB for the rapid development of compounds for the prevention and treatment of coronavirus disease (COVID-19), including a SARS-CoV-2 spike protein-targeting neutralizing antibody (COVI-GUARD), a cocktail of SARS-CoV-2 spike protein-targeting neutralizing antibodies (COVI-SHIELD) and an angiotensin converting enzyme 2 (ACE2) decoy (COVIDTRAP).

"Our wide portfolio of immuno-therapeutic assets is unrivaled in the industry, with each asset individually showing great promise, but when put together, we feel they have the potential to break through the most difficult cancer challenges," said Henry Ji, CEO of Sorrento. "And faced with the unprecedented global challenge of COVID-19, we at Sorrento are working day and night to harness the potential of the G-MAB library to generate therapeutic and protective antibodies of exceptional potential for saving lives."

Sorrento is looking to expand its portfolio of life-changing therapies through collaborations with like-minded partners worldwide.

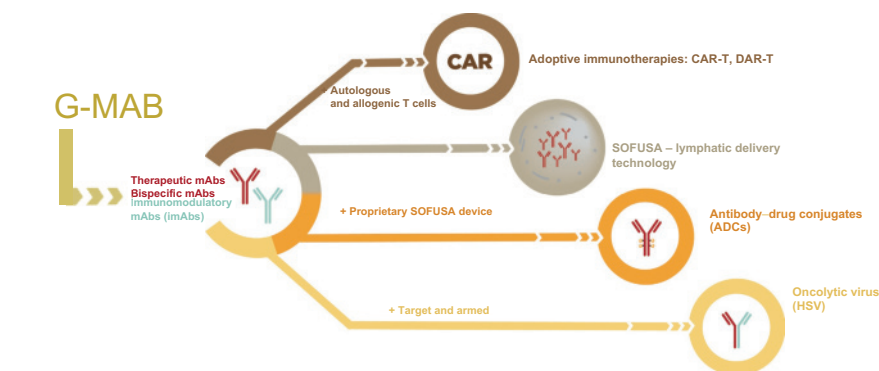


Fig. 1 | Oncology and anti-infective antibodies. Sorrento is developing antibodies against cancer treatment targets including PD-1, PD-L1, CD38, CD123, CD47, VEGFR2 and CD137, and against infectious organisms.

Broad and fully human antibody library

Sorrento has built a deep pipeline of therapeutic, prophylactic and diagnostic binders by harnessing the power of its unique recombinant antibody library, G-MAB. The G-MAB library was built using a proprietary two-step approach to maximize the diversity of naïve donor monoclonal antibodies captured.

First, donor lymphocyte RNAs were amplified using immunoglobulin-specific primers designed to target all five classes of immunoglobulins—IgM, IgG(1-4), IgA, IgD and IgE—and thereby preserve the natural human immunoglobulin diversity. Next, the variable domain regions were selectively and uniformly amplified using a T7 RNA polymerase to create double-stranded cDNAs for insertion into the company's mammalian cell display vectors. The diversity of the heavy chain component of the cDNA library was estimated to be about 7.1×10^7 and that of the light chain component of the library 2.9×10^8 , resulting in a potential combined diversity of about 2.1×10^{16} . The high complexity captured by the G-MAB library maximizes the potential to isolate binders with affinities in the single digit nanomolar or even sub-nanomolar range. The ability to identify antibodies with such high affinities directly from the naïve human antibody pool has the added benefit of eliminating the need for in vitro affinity maturation, a rate-limiting step in the antibody development process.

To date, Sorrento has generated human antibodies against many targets important in cancer treatment, including PD-1, PD-L1, CD38, CD123, CD47, VEGFR2, CD137 and also against critical infectious organisms such as SARS-CoV-2, which are at various stages of development.

Antibody collaborations

The core of Sorrento's technology is provided by its G-MAB recombinant antibody library. This capability is complemented by a full suite of current good manufacturing practice (cGMP)-certified facilities that provide manufacturing, fill/finish and full analytical support capabilities allowing the company to drive drug development from preclinical through investigational new drug (IND) and to late-stage clinical trials.

The facilities include a state-of-the-art cGMP antibody and cell therapy manufacturing unit focused on INDs; a second unit providing aseptic and non-aseptic fill and finish services including lyophilization, labeling/kitting and long-term controlled room temperature, cold and frozen storage; and a viral production unit supporting cell culture, purification, fill and finish processes as well as analytical assay development and quality control testing. In addition to these three California-based units, Sorrento operates an ADC production facility in Suzhou, China, that supports clinical cGMP production of drug linkers as well as antibody conjugation.

These facilities provide Sorrento with a global footprint of capabilities for manufacturing drug substances and drug products for pre-clinical, phase 1 and phase 2 clinical trials, and to deliver life-changing therapies to patients through strong partnerships.

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