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Unlocking The Immune System: A Re-engineered Approach To Treat Cancer

by

The unmet medical need in oncology is changing. While immunotherapies have transformed the treatment of some cancers, they are only available to, and effective in, a small subset of patients. Bringing the power of immunotherapies to more patients is now the defining challenge of oncology R&D. Recognizing that, Alkermes is using R&D capabilities honed over 30 years of work on complex, hard-to-treat diseases to drive a potential next breakthrough in cancer therapy.

Immunotherapies, including checkpoint inhibitors such as pembrolizumab, are highly effective in some patients but durable complete responses remain rare. Only around 12% of patients respond to currently available immunotherapies. Many more patients are ineligible for treatment with immunotherapies, in part because the drugs are not approved for all cancer types. Therefore, only a fraction of patients currently benefit from these treatments.

Physicians need new drugs, or new drug combinations, to overcome this challenge and expand the population of cancer patients who may benefit from immunotherapies, as well as to treat people who progress after treatment with immuno-oncology medicines. The search for potential new drugs and combinations has galvanized researchers in the years since the strengths and limitations of checkpoint inhibitors became clear.

Alkermes has identified the challenge of expanding the impact of immunotherapies as a good fit for its R&D capabilities. In its early years, Alkermes built its expertise in formulation and drug delivery, modifying existing small molecules to develop medicines that could be delivered more safely and efficiently. Alkermes' proprietary technologies were then incorporated into third-party medicines that are commercialized by global pharmaceutical companies, and also led to Alkermes' proprietary products VIVITROL® and ARISTADA®.

However, with its growing R&D and protein engineering capabilities and a keen interest to address complex diseases with high unmet needs, the company evolved its strategic R&D approach to focus on developing novel drugs in both neuroscience and oncology. The most recent success story was the recently launched LYBALVI®.

“There are still millions of patients with complicated and difficult-to-treat health conditions in both neuroscience and neuropsychiatry, as well as oncology, who have limited treatment options available to them. So, we've evolved our patient-focused research and development efforts to focus on developing novel medicines based on validated biological targets, leveraging our advanced medicinal chemistry and protein engineering capabilities,” Dr. Craig Hopkinson, Chief Medical Officer and Executive Vice President, Research & Development at Alkermes, said.

Realizing The Potential Of IL-2

The potential power of Alkermes’ approach may be illustrated by nemvaleukin, the company’s novel, investigational, engineered IL-2 variant immunotherapy. IL-2 may be considered the first immuno-oncology drug. A recombinant form of the cytokine won approval decades ago after showing significant promise in renal cell carcinoma and melanoma, but dose-limiting toxicities prevented its broader use. Alkermes set out to see if it might mitigate the shortcomings.

“Our design hypothesis for nemvaleukin was to build upon the proven anti-tumor activity of high-dose IL-2, while mitigating certain toxicity issues by using a novel design,” Dr. Hopkinson said.

Using its R&D expertise, Alkermes developed a novel investigational version of IL-2 that is a stable, inherently active fusion protein that does not degrade to the native IL-2 and is designed to prevent the activation of the pathways that previously led to IL-2’s toxicities.

The focus on the validated but limited therapeutic use of IL-2 reflects the potential for a better form of the cytokine to be a powerful weapon against cancer and a potential ally to other immunotherapies. Immune cells need to be in and around tumors for checkpoint inhibitors to work but are only present at very limited levels in some patients’ cancers. In such patients, the cells needed to fuel a strong anti-tumor attack are absent, and checkpoint inhibitors cannot work effectively. IL-2 may equip more patients to respond to immunotherapies by activating CD8 T cells and natural killer (NK) cells inside the tumor and in the periphery, while directly driving cancer-fighting mechanisms.

Alkermes’ positioning of nemvaleukin as the drug to possibly realize the potential of IL-2 is built on early evidence that the candidate drives expansion of CD8 T cells and NK cells relative to Tregs.

Encouraging results from clinical trials to date have helped Alkermes to further narrow their focus on investigating difficult-to-treat platinum-resistant ovarian cancer and mucosal melanoma. The company is also studying a wide range of other solid tumors.

“We've really taken the time to study the monotherapy setting, as well as the setting where one would not expect to see checkpoint inhibitor responses and where patients have already progressed. That work makes the program unique,” Dr. Hopkinson said.

Advancing Nemvaleukin Toward Registration

Encouraged by the results, Alkermes is proceeding with potential registrational studies in PROC (named ARTISTRY-7), and melanoma (named ARTISTRY-6), while continuing to research less frequent intravenous (IV) dosing options and explore the potential for subcutaneous dosing. Preclinical studies have helped to further identify the potential for the IL-2 drug to play a vital role in novel combination approaches in oncology as well.

Alkermes is enrolling patients in its registrational programs in melanoma and PROC, having already received FDA fast-track designation in both indications. Beyond melanoma and PROC, the company is looking for partnerships to realize the potential of combination opportunities that the preclinical and clinical data show are possibilities for nemvaleukin.

The progress of nemvaleukin toward registration is part of a broader push by Alkermes into novel medicines. In cancer, Alkermes is applying lessons from nemvaleukin to IL-12 and IL-18 candidates that are in preclinical development. The pipeline also features novel neuroscience candidates.

Alkermes’ drug candidates build on decades of work to improve the treatment of complex, hard-to-treat diseases. As the candidates advance, Alkermes stands to add to earlier successes by tackling significant unmet medical needs in oncology and neuroscience.

Craig Hopkinson, M.D.

Executive Vice President, Research & Development and Chief Medical Officer

Craig Hopkinson, M.D., serves as Alkermes’ Executive
Vice President of Research & Development and Chief Medical Officer. In this role, Dr. Hopkinson leads the company’s Discovery, Pharmaceutical Development, Early Stage Clinical Development,

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Late Stage Clinical Development, Regulatory Affairs, Clinical Operations, PMO and Medical Affairs functions. He is responsible for the strategic development and execution of clinical development programs for the company's pipeline of drug candidates.

Dr. Hopkinson has more than 25 years of experience building and leading clinical development organizations and medical affairs groups. He has led multidisciplinary development teams in a range of therapeutic areas, including neuroscience, oncology, gastroenterology, infectious diseases, cardiovascular conditions, inflammation, genetic diseases, hematology and neurodegenerative diseases. Before joining Alkermes in 2017, Dr. Hopkinson served as Senior Vice President of Medicines Development and Head of Global Medical Affairs at Vertex Pharmaceuticals. Prior to this role, Dr. Hopkinson held various leadership positions at Eisai Pharmaceuticals, Elan Pharmaceuticals, Actelion Pharmaceuticals and Pfizer.

Dr. Hopkinson earned a Bachelor of Medicine and Bachelor of Surgery at the University of the Orange Free State in South Africa.