Ocugen developing therapies for rare and underserved eye diseases

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BIOTUESDAYS by Kilmer Lucas

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Ocugen (NASDAQ:OCGN) is taking a multi-pronged approach to ophthalmology with a diversified pipeline that includes a breakthrough modifier gene therapy platform, novel biologics and small molecules, targeting a broad range of high-need retinal and ocular surface diseases.

“Since Ocugen’s founding, we have sought to develop innovative therapies to treat rare and underserved eye diseases through a combination of therapeutic approaches,” Shankar Musunuri, chairman, CEO and co-founder, says in an interview with BioTuesdays.

The company’s most advanced drug candidate, OCU300, is an orphan drug candidate for ocular graft versus host disease (oGVHD), in a Phase 3 clinical trial. The trial was 50% enrolled in December, with top-line data release set for the second half of 2020.

In its preclinical program, Ocugen’s gene therapy platform is addressing inherited retinal degeneration disorders and dry age-related macular degeneration (AMD). OCU400 is based on the nuclear hormone receptor gene, NR2E3, and has received two orphan drug designations targeting two distinct inherited retinal degeneration diseases. OCU410 is based on the RORA gene for the treatment of dry AMD.

Looking beyond rare eye diseases, OCU200, Ocugen’s novel biological product candidate is a fusion protein of human transferrin and tumstatin that acts through a distinct mechanism of action. OCU200 could support the company’s expansion into mass ophthalmological indications, such as wet AMD, a leading cause of blindness in the elderly; diabetic macular edema; and diabetic retinopathy, which have a total U.S. prevalence of some 10 million patients.

Ocugen’s IP is protected with 31 issued U.S. and foreign patents and 34 U.S. and foreign patent applications. The company went public in September 2019 through a reverse merger with Histogenics.

oGVHD is an autoimmune disease that affects some 60% of patients that undergo an allogeneic bone marrow transplant, resulting in a market of about 63,000 patients in 2020. Dr. Musunuri suggests that oGVHD can develop in three-to-six months after a transplant as donor-derived leukocytes attack recipient ocular tissue. Patients encounter dry, tearless eyes, vision issues, severe pain, discomfort, and potential ocular scarring, which may lead to significant vision loss and irreparable ocular surface damage.

“Ocugen is the first and only company to receive orphan drug designation from the FDA for the treatment of oGVHD,” Dr. Musunuri says.

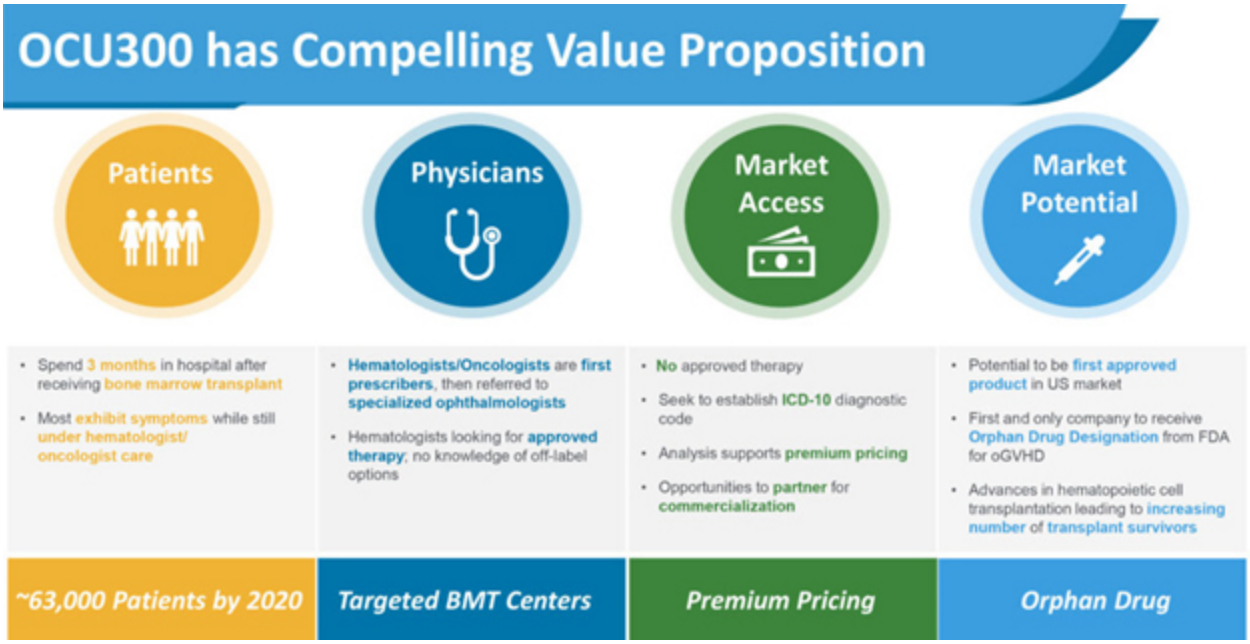
In its first Phase 3 study with OCU300, Ocugen is enrolling 60 patients, randomized two-to-one, in an 84-day study at more than 10 bone marrow transplant centers in the U.S. The co-primary endpoints include ocular discomfort based on a 10-point Visual Analog Scale and ocular redness based a Validated Bulbar Redness Score.

Dr. Musunuri notes that the active pharmaceutical ingredient in OCU300 is brimonidine, which has been approved for chronic treatment of glaucoma. “Our 505(b)(2) regulatory pathway allows us to use the established safety data already available for brimonidine.”

However, generic brimonidine is not approved for oGVHD, he adds. “OCU300 has a different formulation, is preservative-free and does not contain benzalkonium chloride, which is damaging to the cornea.”

Dr. Musunuri says drug delivery to the lacrimal gland from traditional eye drops is low relative to other target tissues. “Our OcuNanoE drug delivery system increases brimonidine delivery to the lacrimal gland and improves overall efficacy of OCU300.”

Citing OCU300’s compelling value proposition, he contends that patients may begin to exhibit symptoms of oGVHD while still in the hospital, under the care of a hematologist or oncologist, who are often the first prescribers and do not have approved therapies for patients. Ocugen also is seeking to establish an ICD-10 diagnostic code for OCU300, which would streamline the reimbursement process and provide more data to physicians.



In Ocugen's breakthrough modifier gene therapy platform, Dr. Musunuri contends that OCU400 has demonstrated the ability, in preclinical studies, to stop progression of many inherited retinal diseases and potentially act as a transformative therapy.

The platform differentiates itself from gene augmentation by introducing a functional gene to modify the expression of many genes and gene networks, compared with gene augmentation, which targets one individual gene mutation at a time and one disease, he adds.

"Our novel approach is based on nuclear hormone genes, which regulate multiple functions within the retina and has the potential to target multiple diseases with one product, allowing us to recoup development costs over multiple therapeutic indications."

In September 2019, Ocugen cleared a major hurdle in the manufacturing bottleneck faced by gene therapy developers. The company inked a strategic partnership with CanSino Biologics of China to provide all development and clinical supplies for OCU400 as well as an option to support commercial manufacturing for Ocugen. The accord also gives commercialization rights to CanSino in greater China.

"This partnership paves a path for us to advance OCU400 into the clinic with significantly reduced capital needs," Dr. Musunuri points out. Ocugen plans to continue IND-enabling studies with OCU400 this year and begin a Phase 1/2a clinical trial in 2021.

Those clinical timelines also extend to OCU200, Ocugen's preclinical biologic for the treatment of wet AMD, diabetic macular edema and diabetic retinopathy, where patients are seeking new therapies beyond anti-vascular endothelial growth factor (VEGF) injections.

According to Dr. Musunuri, 30% to 50% of patients are non-responders to anti-VEGF injections. VEGF produces new blood vessels when the body needs them. But too much VEGF can lead to growth of abnormal blood vessels in the eye, damaging vision and leading to blindness.

OCU200 has been designed to selectively work on active endothelial cells, inhibiting new blood vessel formation and reducing damage to the retina. In preclinical studies, OCU200 demonstrated superior efficacy with potentially fewer injections in head-to-head studies against anti-VEGF therapies.

"We think OCU200 has the potential to be an important new therapy for millions of patients with underserved eye diseases," Dr. Musunuri adds.

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