Aerie Completes Enrollment of Phase 3 Registration Trial of Rhopressa

Aerie Pharmaceuticals completed enrollment of the company's 400-patient phase 3 registration trial (Rocket 1) of Rhopressa, according to a company news release. The once-daily, triple-action eye drop is being tested for its ability to lower IOP in patients with glaucoma or ocular hypertension.

According to Aerie, if approved, Rhopressa would become the only once-daily product available that specifically targets the trabecular meshwork. Preclinical results have demonstrated that the drug also lowers episcleral venous pressure, which contributes approximately half the IOP in healthy subjects, the news release said. Further, the drug reportedly has an additional mechanism that reduces the production of fluid in the eye and thus lowers IOP. Biochemically, Rhopressa is known to inhibit both Rho kinase and norepinephrine transporter.

Rocket 1 and a second phase 3 registration trial (Rocket 2) will measure efficacy over 3 months. The primary efficacy endpoint of the trials is to demonstrate noninferiority of IOP lowering for Rhopressa compared to timolol. Additionally, the company is conducting a safety-only study in Canada named Rocket 3.

"We are delighted to report that patient enrollment for Rocket 1 has been completed ahead of our expectations," Vicente Anido Jr, PhD, chairman and CEO of Aerie, said in the news release. "Further, Rocket 2 enrollment remains fully on schedule. The accelerated enrollment of Rocket 1 is a testament to the continued high level of interest in Rhopressa we have experienced from the ophthalmology community."

In the company's phase 2b clinical trial, which was successfully completed in May 2013, Rhopressa reportedly demonstrated a strong IOP-lowering effect, with mean reductions of 5.7 and 6.2 mm Hg on days 28 and 14, respectively. Additionally, the drug demonstrated a consistent mean IOP-lowering effect irrespective of the patients' baseline IOPs. According to the company, this finding differentiates Rhopressa from currently marketed IOP-lowering prostaglandin analogues and β-blockers, which have their greatest effect at higher baseline IOPs but lose efficacy as the baseline diminishes, as shown in published studies. In the Roclatan phase 2b trial completed in June 2014, Rhopressa performed with similar results as in its phase 2b trial completed in May 2013 and demonstrated additive efficacy when used in combination with latanoprost.

Pending the continued advance of the Rhopressa phase 3 program and regulatory approvals, Aerie said it intends to commercialize the drug in North American markets and possibly Europe with its own sales force and will seek commercialization partners in other key territories, including Japan and possibly Europe. Three-month efficacy results are expected by mid-2015, and if the trials are successful, the company said it expects to submit a new drug application filing by mid-2016.

SLT Effective for the Treatment of Primary Angle-Closure Glaucoma

Selective laser trabeculoplasty (SLT) is an effective short-term treatment for primary angle-closure glaucoma, although complete success is more common with a prostaglandin analogue, according to a study in *JAMA Ophthalmology*.[1]

The investigators compared the efficacy of SLT with that of travoprost 0.004% (Travatan; Alcon) over 6 months. A total of 100 patients who developed recurrent primary angle-closure glaucoma after laser peripheral iridotomy and in whom the angles had opened at least 180° were randomly assigned to receive therapy with SLT or the prostaglandin analogue. Forty-nine patients in the SLT group and 47 in the prostaglandin analogue group completed the study; 14 of 49 eyes (28.6%) underwent SLT twice.

According to the study, at 6 months, the mean IOP had decreased by an average of 4 mm Hg in the SLT group and by 4.2 mm Hg in the prostaglandin analogue group ($P = .78$). Complete success (IOP ≤ 21 mm Hg without additional IOP-lowering medication) was achieved by 60% of eyes in the SLT group and by 84% of eyes in the prostaglandin analogue group ($P = .008$). There was no significant difference in failure rates between the SLT and prostaglandin analogue groups (22% vs 10%, respectively; $P = .10$).

Even though improvement was slightly greater in the prostaglandin analogue group, "these findings substantiate the potential role of SLT in a subset of angle-closure

disease and also open an alternative strategy to manage increased IOP amidst growing concerns of poor adherence, increasing cost, and unsatisfactory quality of life associated with long-term medical therapy," the investigators concluded.

The study was supported by Ellex, which sells two SLT laser models.

1. Narayanaswamy A, Leung CK, Istiantoro DV, et al. Efficacy of selective laser trabeculoplasty in primary angle-closure glaucoma: a randomized clinical trial [published online ahead of print November 27, 2014]. *JAMA Ophthalmol.* doi:10.1001/jamaophthalmol.2014.4893.

First Surgeries Performed in Spain With the InnFocus MicroShunt

The first two surgeries using the InnFocus MicroShunt (InnFocus) were conducted at the Hospital Clinico San Carlos in Madrid, according to a news release.

"The surgeries went very well, and the patients are showing good results," surgeon Julian Garcia Feijoom, MD, PhD, said in the news release. "We believe that the InnFocus MicroShunt, and its less invasive way to treat glaucoma, will help patients around the world."

The device consists of a microtube that is about twice the size of an eyelash. The company's goal is to provide a safe, effective, stable, and easy treatment for early- to late-stage glaucoma. According to InnFocus, the patented microshunt is made from the innovative SIBS Material to control flow.

The company said it expects to treat approximately 150 glaucoma patients by early 2015. The device is currently in phase 1 FDA trials at 12 centers in the United States, and the company plans to begin the final FDA phase in 2015. Patients have also been treated with the InnFocus MicroShunt in France, Spain, Japan, and the Dominican Republic. The device has been implanted alone or in combination with cataract surgery in clinical trials outside the United States in patients with glaucoma ranging from early to late stage.

According to the news release, 70 patients implanted with the device experienced a significant and stable reduction in mean IOP to below 14 mm Hg for up to 3 years.

NIH Funds Optometrists to Improve Glaucoma Treatment

The National Institutes of Health awarded two professors at the Indiana University School of Optometry a $1.4 million grant to advance innovations toward overcoming longstanding barriers to the development of new treatments for glaucoma, according to a news release.

William H. Swanson, PhD, will lead a collaboration with Stephen A. Burns, PhD, that uses Dr. Swanson's advances in neural modeling and visual psychophysics and Dr. Burns' improvements in the diagnostic imaging of the retina to develop better methods for diagnosing and assessing the progression of glaucoma. By measuring ganglion cell loss via three-dimensional analysis of the retinal nerve fiber layer (RNFL), they hope to better explain the processes by which aging and disease affect the RNFL. Current measures of the effects of ganglion cell death have been based on the thickness of the RNFL rather than on the entire structure of the layer, the news release said.

Because retinal ganglion cell numbers, and therefore fiber layer thickness, can vary as much as twofold among any given age group of healthy people, "it is difficult to detect early stages of the disease from what is often seen as normal variability in healthy people," Dr. Swanson said. "What we are doing that is new is measuring the entire structure of the retinal nerve fiber layer, which is less variable from subject to subject. Our goal is that the doctor will be able to take a picture of the back of the eye showing where the retinal nerve fiber layer structure is abnormal. That image could then be used to guide the doctor to test corresponding locations with perimetry."

Dr. Burns and colleagues developed a wide-field adaptive optics scanning laser ophthalmoscope that allows high-resolution imaging of the RNFL and overcomes imaging barriers in aging eyes. Dr. Swanson and colleagues developed a new form of perimetry that reduces between-subject variability in people free of glaucoma and in-subject variability in glaucoma patients. Together, the two teams will use Dr. Burns' custom-designed ophthalmoscope along with spectral-domain optical coherence tomography to perform high-resolution imaging of the RNFL. Spectral-domain optical coherence tomography is typically used to measure the layer's thickness, but a special agreement with Heidelberg Engineering will reportedly allow Drs. Swanson and Burns to customize and export raw data that traditionally would have had limited applications for their research.

"Our first step is to reduce spurious features produced in image acquisition by using a custom [three-dimensional] segmentation process," Dr. Swanson said. "The second step will be to produce images that encode angle and density of fibers by using steerable

spatial filters to identify individual nerve fibers." In the future, clinicians may be able to use these new images to conduct more precise testing through better detection of damaged areas.

Centers for Medicare & Medicaid Services Renews Mitosol Reimbursement

Mobius Therapeutics received a renewal of reimbursement for Mitosol (mitomycin for solution) Kit for Ophthalmic Use in 2015. According to a news release, Mitosol will continue to receive a separate, pass-through reimbursement at 106% of the average sales price. The full updated reimbursement schedule for hospital outpatient prospective payment may be viewed at http://go.cms.gov/14A11pk. The published rate for reimbursement of J7315 as of January 1, 2015, is $372.80.

"As Mitosol remains the only approved formulation of mitomycin C bearing an ophthalmic indication, this continuation of reimbursement supports federal regulatory guidance related to the use of approved formulations," Ed Timm, president and CEO of Mobius Therapeutics, said in a news release. "When regulatory guidance and economics align, patients and providers win. As Medicare payment remains unchallenged, we are seeing broad adoption of this same payment policy from private payors. This reaffirmation will assure existing and new Mitosol patients and providers economic security. Access to Mitosol will meet their ongoing needs, both clinical and financial."

Online Survey Results November/December 2014

How often do you encounter non-English-speaking patients at your practice?

Regularly	64.29%
Sometimes	14.29%
Rarely	21.43%
Never	0

Based on your experience, which approach has been most effective for cultivating relationships with non-English-speaking patients?

Use capable members of the staff to serve as translators	78.57%
Hire interpreters on an as-needed basis	14.29%
Use translation phone services	7.14%
Use a mobile phone app	0

How important do you think genetic testing is in glaucoma?

Very	36.84%
Somewhat	21.05%
Not very	42.11%

Do you believe its importance will grow in the future?

Yes	89.47%
No	10.53%

Travatan Approved in Europe for Pediatric Indication

Travoprost (Travatan 40 µg/mL; Alcon) has been granted an additional indication by the European Commission to decrease elevated IOP in patients aged 2 months to less than 18 years who have ocular hypertension or pediatric glaucoma, according to a news release. The eye drop is currently indicated for IOP reduction in adults with ocular hypertension or open-angle glaucoma.

"Pediatric glaucoma affects only a small number of children worldwide, so there is little data available about how to manage this sight-threatening disease in pediatric patients," Professor Stefano Gandolfi, MD, head of the Eye Clinic, University of Parma, Italy, said in a news release. "The Travatan approval for this additional indication means that ophthalmologists now have a new medicine to prescribe to help children and adolescents control their IOP level every day."

The approval is based on a 12-week, phase 3, multicenter, double-masked, randomized, parallel-group study (N = 152) that compared travoprost and timolol. The primary efficacy endpoint was the change in IOP from baseline to week 12. According to Alcon, travoprost's effect on IOP was observed in patients after the second week of treatment and was consistently maintained throughout the study. Reductions in mean IOP in the travoprost and timolol groups were similar. The adult dose of travoprost was shown to be safe and effective for use in children aged from 2 months to less than 18 years. No data are available for children below the age of 2 months. The most frequently reported adverse drug reactions in pediatric patients were ocular hyperemia and eyelash growth. ■