A Novel, First-in-Class Investigational Treatment for Acquired Blepharoptosis

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Disclosure: David Jacobs, MD, MBA, is an employee of Osmotica Pharmaceutical US LLC and has equity interest in its parent, Osmotica Pharmaceuticals plc.

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What is Blepharoptosis?

Blepharoptosis (ptosis or droopy eyelid)
Abnormal low-lying upper eyelid margin with the eye in primary gaze

► Millions affected in the U.S. and worldwide*
► Untreated blepharoptosis impacts function (peripheral visual field loss) and appearance (reduced confidence in social settings) and can affect activities of daily living1-3

The investigational agent RVL-1201 is the first potential pharmacologic treatment for acquired blepharoptosis

* While no robust epidemiological studies exploring the prevalence of blepharoptosis in the markets outlined above, we believe it is a common condition affecting millions of Americans. Although we believe the numbers presented above reflect the approximate potential market opportunity based on our research and available market information, there is no assurance that the market opportunity will not differ from such numbers and such difference could be material.

There is a Significant Unmet Need for Non-Surgical Treatment Options for Acquired Blepharoptosis

► Acquired blepharoptosis is commonly associated with aging

► Significant clinical need for effective, non-invasive therapeutic option
  
  • Most patients go untreated — standard of care is surgery
  
  • Surgery usually reserved for most severe cases with largest functional impact, involves significant time, cost, and risk of complications

  • <3% of patients with blepharoptosis in U.S. are treated each year

RVL-1201 Overview

► Phase 3 trials completed
► Toxicology and long-term safety work completed
► Exploring partnerships for international availability and distribution in the EU and Asia
► NDA submitted September 2019

► Oxymetazoline HCL ophthalmic solution, 0.1%
► Formulated with a unique polymer designed to be soothing to the eye

► Direct-acting α-adrenergic receptor agonist with well-established efficacy and safety profile
► Stimulates contraction of Müller’s muscle, raising the upper eyelid


MOA, mechanism of action
# RVL-1201 Phase 3 Clinical Program

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**Design**
- RVL-1201-201: Randomized, multicenter, double-masked, placebo-controlled
- RVL-1201-202: Randomized, multicenter, double-masked, placebo-controlled
- RVL-1201-203: Randomized, multicenter, double-masked, placebo-controlled

**Duration**
- RVL-1201-201: 6 weeks
- RVL-1201-202: 6 weeks
- RVL-1201-203: 12 weeks

**Outcomes**
- **Primary efficacy:** CFB in number of points seen in top 4 rows of LPFT
- **Secondary efficacy:** CFB in MRD-1
- **Safety**

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CFB, change from baseline; LPFT, Leicester Peripheral Field Test; MRD-1, Marginal Reflex Distance
Efficacy Endpoints, RVL-1201 Phase 3 Trials

Primary efficacy endpoint
► The LPFT, a customized visual field test designed specifically to assess superior visual field loss due to ptosis,¹ was performed using an HVF analyzer
► 35 points (in the 4 rows at or above 10° from fixation) tested in the superior field
► LPFT score tallied based on the total number of points seen in the top 4 rows

Secondary efficacy endpoint
► MRD-1 is the distance between the center of the pupillary light reflex and the upper eyelid margin with the eye in primary gaze
► Normal MRD-1 is 4-5 mm

HVF, Humphrey Visual Field; LPFT, Leicester Peripheral Field Test; MRD-1, Marginal Reflex Distance
Primary Efficacy Endpoint: Improvement on the LPFT
Combined Efficacy Studies (RVL-1201-201, RVL-1201-202)

Increase in points seen on LPFT = improvement in superior (upper) visual field

* vs. vehicle, from an ANCOVA model with study and treatment as fixed factors and baseline score as a covariate
LPFT, Leicester Peripheral Field Test.
Secondary Efficacy Endpoint: Improvement in MRD-1 Combined Efficacy Studies (RVL-1201-201, RVL-1201-202)

* vs. vehicle, from an ANCOVA model with study and treatment as fixed factors and baseline score as a covariate

MRD-1, Marginal Reflex Distance

Mean (SD) change from baseline in MRD-1

- Day 1 (6 hours post-instillation)
- Day 14 (2 hours post-instillation)

RVL-1201 (n=203)
Vehicle (n=101)

▲ Increase in MRD-1 = greater elevation of the upper eyelid

p<0.0001
Secondary Efficacy Endpoint: Improvement in MRD-1

Rapid and sustained effect after application

Significant effect vs. vehicle at 5 minutes and 6 hours after drop application

* vs. vehicle, from an ANCOVA model with treatment as a fixed factor and baseline score as a covariate

MRD-1, Marginal Reflex Distance
RVL-1201 Efficacy

Before RVL-1201 dose

After RVL-1201 dose

Before RVL-1201 dose

After RVL-1201 dose
RVL-1201 Efficacy

Before RVL-1201 dose

After RVL-1201 dose

Before RVL-1201 dose

After RVL-1201 dose
RVL-1201 Safety and Tolerability

- Overall, treatment-emergent adverse events (AEs) were reported for 31.2% of subjects receiving RVL-1201 and 30.6% of subjects receiving vehicle.
  - Most AEs were **mild and did not require treatment**
  - **AEs resulting in treatment discontinuation were uncommon** in subjects receiving RVL-1201 (n=3/94 and n=1/109 subjects in the two 6-week efficacy studies, respectively; n=5/157 subjects in the 12-week safety study)
  - No AE occurred in more than 3.5% of subjects receiving RVL-1201

- Tolerability assessed in 12-wk Ph 3 safety trial
  - 92.0% of subjects rated RVL-1201 as causing no discomfort, while 8% rated it as causing minimal discomfort.
Conclusions

► Non-surgical treatment of acquired blepharoptosis represents a large unmet need and significant commercial opportunity

► The investigational therapeutic RVL-1201 (oxymetazoline HCL ophthalmic solution, 0.1%) was safe and effective in clinical trials, and is a potential non-invasive treatment option for acquired blepharoptosis

► RVL-1201, upon approval, has the potential to change how ptosis is treated in patients worldwide
Vertical Pharmaceuticals, LLC

- Division of Osmotica Pharmaceuticals plc, a fully integrated and diversified biopharmaceutical company headquartered in Bridgewater, New Jersey

- Vertical currently markets branded Rx and OTC products in women’s health and neuroscience

- Proprietary ER platform enables delivery of novel formulations to new targets

Strategic focus: Deliver a diversified portfolio of specialty products to improve the lives of patients burdened by substantial unmet needs

If approved, RVL-1201 will be a first-in-class advancement in the treatment paradigm for acquired blepharoptosis