Establishing a Translational Read-Through Approach for Inherited Retinal Disorders

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Forward-Looking Statements

This presentation contains forward-looking statements, which are generally statements that are not historical facts. Forward-looking statements can be identified by the words "expects," "anticipates," "believes," "intends," "estimates," "plans," "will," "outlook" and similar expressions. Forward-looking statements are based on management's current plans, estimates, assumptions and projections, and speak only as of the date they are made. We undertake no obligation to update any forward-looking statement in light of new information or future events, except as otherwise required by law. Forward-looking statements involve inherent risks and uncertainties, most of which are difficult to predict and are generally beyond our control. Actual results or outcomes may differ materially from those implied by the forward-looking statements as a result of the impact of a number of factors, including: the development of the Company’s read-through technology; the approval of the Company’s patent applications; the Company’s ability to successfully defend its intellectual property or obtain necessary licenses at a cost acceptable to the Company, if at all; the successful implementation of the Company’s research and development programs and collaborations; the Company’s ability to obtain applicable regulatory approvals for its current and future product candidates; the acceptance by the market of the Company’s products should they receive regulatory approval; the timing and success of the Company’s preliminary studies, preclinical research, clinical trials, and related regulatory filings; the ability of the Company to consummate additional financings as needed; as well as those discussed in more detail in our Annual Report on Form 10-K and our other reports filed with the Securities and Exchange Commission.
# Large Unmet Need in Inherited Retinal Disorders

<table>
<thead>
<tr>
<th></th>
<th>Incidence</th>
<th>US Prevalence</th>
<th>Nonsense Proportion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Usher Syndrome</td>
<td>3.2-6.2/100K</td>
<td>16.3K</td>
<td>20%</td>
</tr>
<tr>
<td>Retinitis Pigmentosa</td>
<td>1-5/10K</td>
<td>67K</td>
<td>15-50%</td>
</tr>
<tr>
<td>Choroideremia</td>
<td>1-9/100K</td>
<td>6.5K</td>
<td>36%</td>
</tr>
<tr>
<td>Stickler Syndrome</td>
<td>1-9/100K</td>
<td>66K</td>
<td>20%</td>
</tr>
</tbody>
</table>

Population values from National Organization for Rare Disorders (NORD) and Orphanet
What Causes Usher Syndrome?

• Usher syndrome is inherited
• It passes from parents to a child through genes
• Sometimes genes are altered, or mutated
What are Genetic Mutations?

- Genetic mutations are errors in our DNA code.
- They cause cells in our body to behave abnormally.
Mutations and Proteins

• Some mutations cause proteins to be shorter than usual
• These shorter proteins do not work properly
• Many patients have Usher Syndrome due to shorter proteins

![Diagram showing full protein and mutation](image-url)
Focus on Restoring Protein Function

Eloxx drug is proposed to work by read-through process

Mutated Protein

Full Protein
Glycoside-Based Approach

- Gentamicin is an antibiotic of the glycoside family
- Glycosides promote read-through some but have side effects
- Eloxx is developing specific glycosides, known as eukaryotic ribosomal selective glycosides (ERSGs) that are better tolerated and have greater ability to restore protein function, as a potential treatment for Usher Syndrome
In this study, compared to gentamicin, Eloxx drug did not negatively affect photoreceptors – the light sensing cells in the retina.

Figures: Photopic electroretinograms (ERGs) from normal rabbits and rabbits dosed intravitreally with 300 μg gentamicin or Eloxx drug.
Increased Full-Size Protein Production in Cells With an Usher Syndrome Mutation

Figure: Effects of gentamicin (4 mM) and Eloxx drugs (1.5 mM) on read-through activity in cells with the Ush2A R626X mutation assessed using a plasmid-based dual-luciferase assay.
Delivery of Drug to the Retina

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Figure: Ocular tissue concentrations of Eloxx drug three hours after intravitreal injection in rabbits
Emerging Profile of Read-through For Usher Syndrome

SAFETY: Tolerability
At doses >10-fold over anticipated treatment level

EFFECT: Read-through of Usher mutations >gentamicin

DISEASE LOCATION: Pharmacokinetics demonstrate substantial retinal exposure

GOAL: Focus on developing therapies to prevent blindness
THANK YOU