On July 18, 2022, the Food and Drug Administration (FDA) tentatively approved LUMRYZ™ (sodium oxybate) for extended-release oral suspension for the treatment of excessive daytime sleepiness or cataplexy in adults with narcolepsy

As described in the FDA letter, the review of the LUMRYZ New Drug Application is complete

- **Final approval is subject to a June 2023 patent expiry**
- Final approval may not be granted before the patent has expired or is otherwise disposed of

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Why is FDA involved in a patent issue?

- The LUMRYZ New Drug Application was a 505(b)(2) submission, which is a streamlined application referencing a drug previously approved by the FDA (i.e., Xyrem®[1], which was initially FDA approved in 2002)
- When 505(b)(2) NDAs are submitted, FDA reviews the *"Approved Drug Products with Therapeutic Equivalence Evaluations"*, known commonly as the Orange Book, to determine whether there are any patents on the reference drug
    - Only patents pertaining to the drug substance (active ingredient), the drug product (formulation or composition), or the method of using a drug can be listed in FDA's Orange Book
- Applicants who submit a Paragraph IV certification state that they believe a patent is *"invalid, unenforceable, or will not be infringed"* by the applicant's product
    - Upon a Paragraph IV certification, the Applicant notifies the patent owner; if the patent owner initiates an infringement action within 45 days of that notice, FDA must delay final approval of the application for a period of up 30 months from the date the lawsuit is initiated (assuming no earlier expiration or other legal disposition of the patent)

What is the patent blocking final approval of LUMRYZ?

- US Patent No. 8,731,963 (the "'963 patent") is the patent that currently stands in the way of a final approval
- The '963 patent has a Use Code listed in FDA's Orange Book for Xyrem[1] describing the patent as a:
    - *"Method of treating a patient with a prescription drug using a computer database in a computer system for distribution"*
        - The '963 patent is due to expire (including the pediatric exclusivity patent term extension) on **June 17, 2023**

Why does FDA view this patent to be valid and properly Orange Book-listed?

- FDA only has a ministerial role in listing patent information in the Orange Book and does not evaluate validity
- FDA does not review patents for appropriateness of Orange Book listing or whether corresponding Use Codes accurately describe the patent

Is it unusual to patent a REMS?

- Yes, it is unusual to patent a REMS; currently, there are 62 medications that require a REMS; among these, it appears that only 3 medications, one of which is Xyrem[1], have at least one Orange Book listed REMS patent
- It's important to remember the purpose of a REMS, or Risk Evaluation and Mitigation Strategy: these are safety programs the FDA **requires** for certain medications having serious safety concerns to help ensure the benefits of the medication outweigh its risks

- More information about problems with patenting REMS, including proposed solutions for Congress to pass, is available here

Why didn't Avadel prepare for this to happen?

- The LUMRYZ NDA initially included a patent statement and labeling that carved out the '963 patent and explained the rationale for why it should not be a deterrent to FDA approval
- Avadel disagrees with FDA's decision to require certification to the '963 patent and is executing upon several strategies to accelerate potential final approval prior to expiration of that patent in June of 2023

What happens next for LUMRYZ?

- Avadel remains fully committed to bringing LUMRYZ to final approval and availability for patients
- With a tentative approval, the FDA has determined that LUMRYZ meets the standards for safety, efficacy, and manufacturing quality
- **A tentative approval does not allow the medication to be marketed or promoted; the same pre-approval restrictions continue to apply**
- We believe the narcolepsy community deserves access to a once-at-bedtime oxybate medication, and will work diligently to obtain final FDA approval earlier than the June 2023 expiration of the '963 patent

[1] XYREM is a registered trademark of Jazz Pharmaceuticals, Inc.