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Case Study

Streamlining Study Trial Submissions for Success:

An Integrated Summary of Safety (ISS) Case Study with Urovant Sciences



Project Background

Clinical research and drug development relies on partnerships and collaboration more than ever before. Urovant Sciences acquired the Vibegron assets midway through its development process including numerous legacy data sets and an ongoing Phase III study. To achieve the ambitious regulatory submission timeline, set forth by Urovant leadership, the development team needed to partner with an experienced clinical data and statistical programming provider. Working with eClinical Solutions on the regulatory submissions and using the elluminate® Clinical Data Cloud as a centralized data repository, Urovant was able to achieve their submission timelines stretch goals that resulted in an approval for Gemtesa.

Preparing for Submission

The development of Vibegron—a treatment of overactive bladder (OAB) condition in adults—began in 2017. Urovant acquired these asset and data, then submitted their NDA in 2019, aiming to get FDA approval by 2020. The submission package deliverable was an ambitious, eight-month timeline. For successful submission, there were a few hurdles that they needed to prepare for:

- Conversion of 17 legacy studies that were inherited to be SDS compliant
- Conversion of three legacy studies to the latest CDISC data standards
- Three ongoing studies: One in Phase 1 and two in Phase 3
- ISS scope: Integration of six studies using a complex pooling system, and the submission of ISS and individual studies with over 600 outputs

Submission Data Challenges

There were substantial challenges to preparing the 17 legacy studies for submission and aligning them with the ongoing studies that Urovant was performing. The legacy studies needed to be converted to SDS, along with relevant data and documentation. Conversion to SDS also required the creation of the TS trial summary domain, the SDTM annotated CRF, and a defined PDF. Since the TS domain requires deep

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- Founded in 2017
- Headquartered in Irvine, CA
- Focused on developing and commercializing innovative therapies for a range of urologic conditions

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Products Utilized

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Success highlights

1. Submission-ready integrated SDTM and ADaM-compliant data
2. FDA approval in December 2020

understanding of the parameters of the study, creating these sets was challenging. Additionally, all data issues in the legacy studies needed to be adjusted or explained.

Urovant was also working with multiple vendors on the studies and needed a final statistical analytics plan that aligned across these studies. To access and harmonize ADaM and SDTM data, they had built-in dry runs for all ongoing studies. This allowed them to gain access to the raw SDTM data in order to identify issues such as non-conformance.

Choosing an ISS Partner

To meet these goals and be prepared for submission, Urovant needed to find a statistical programming and analysis partner that was experienced and understood their goals. They wanted a team with a proven track record of submission experience, and the ability to deliver quality results on time. The project required expert statistical and programming support, knowledge of CDISC standards, and the ability to be flexible in the face of challenges.

Urovant turned to eClinical Solutions, taking advantage of their expert clinical programming team and lead statisticians. Together, they aligned on strategy, which included weekly calls to create a stream of constant communication with the dedicated and highly experienced eClinical team. This partnership helped the Urovant and eClinical teams function as a single unit, not in the traditional vendor-sponsor relationship, to meet ambitious timelines.

As soon as data became standardized and available from the legacy studies, the eClinical team performed an inventory and gap analysis of the data and documentation that existed. This allowed for Urovant and eClinical to identify issues early on. They also created intelligent batching of deliverables and timing to improve timelines.

Finally, with individual studies being run by other vendors, they performed submission package dry runs as data was received. This allowed them to notice issues up front and fix them quickly in order to proceed. Dry runs also gave the joint team extra time to review data and the medical writing team more time for additional requests, while allowing them to start the writing process sooner. With these processes in place, they were able to meet their timelines.

Results and Lessons Learned

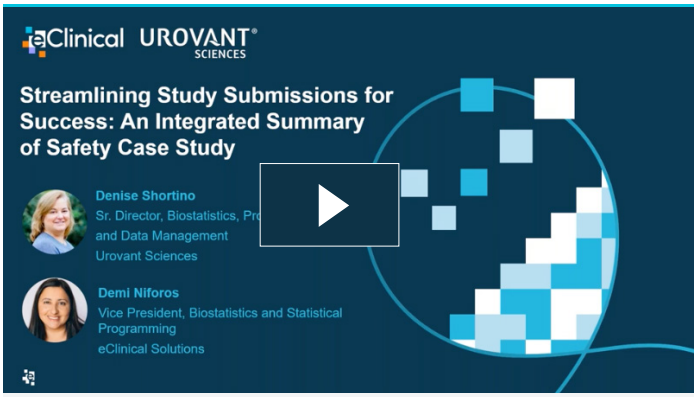
The NDA submission for Vibrogen to treat OAB was submitted at the end of 2019 and received FDA approval in December 2020. The ISS package that eClinical and Urovant collaborated on included:

- Submission-ready integrated SDTM and ADaM-compliant data
- TLF outputs
- Statistical analysis plan
- BIMO packages
- eTMF documentation
- Expedited responses to regulatory inquiries

Lessons Learned

- Regularly test submissions and incorporate dry runs are key to a successful final submission and faster approval.
- Front-load the processes, with multiple ongoing studies, get the bulk of the work done when there is time, instead of competing against multiple projects and deadlines and inquiries from other teams
- Choose the right ISS/ISE partner for your team and business - face-to-face planning was key in creating a collaborative environment where statistics, programming, and medical writing worked together to achieve clear goals.

Along with a well-documented and well-defined plan, eClinical's experienced biostatistics team created an efficient and successful submissions process to gain approval for Urovant Gemtesa.



This presentation originally appeared on Xtalks and features Demi Niforos, VP of Biostatistics and Statistical Programming at eClinical Solutions, and Denise Shortino, Senior Director of Biostats, Programming, and Data Management at Urovant Sciences.

Watch Presentation

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