PROCYSBI™ Approved with Cytel Support

Raptor entrusts data analytics and medical writing to Cytel

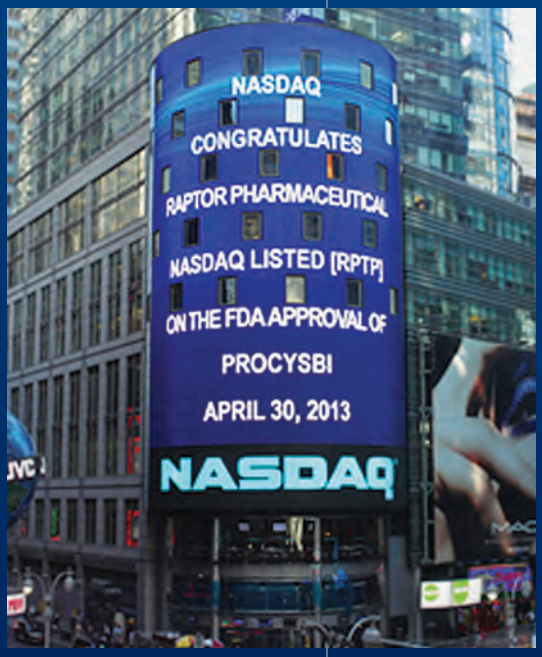
Disease area: Nephropathic cystinosis, a rare but severe metabolic disease affecting children

Trial design: Adaptive non-inferiority trial with unblinded sample size re-estimation (SSR) at interim analysis

Data services: CDISC migration, ADaM development, ISS/ISE SAP & programming, CSR and ISS/ISE medical writing

Challenge

Raptor Pharmaceuticals was seeking FDA approval and orphan drug exclusivity protection of PROCYSBI™ (cysteamine bitartrate) for treatment of nephropathic cystinosis, a rare but serious genetic disorder that affects children. With fewer than 2,000 treatment candidates available worldwide for the pivotal stage, the disease presented a sample size challenge common in orphan therapy development.



Six total studies in North America and Europe were planned in preparation for FDA and EMA NDA filings, when an FDA Special Protocol Assessment (SPA) unexpectedly called for a complete redesign of the planned pivotal trial design.

Raptor needed to respond swiftly — PROCYSBI was their first drug to enter Phase 3 and final development was contingent on continued funding. They enlisted Cytel first to address the FDA's recommendation that the trial demonstrate non-inferiority, despite challenges of a small patient pool.

While managing changes to the statistical design and analysis plan, Raptor was simultaneously sourcing the requisite clinical data management services, biostats and programming, and medical reporting to support the studies and prepare for NDA submission.

"We learned that ongoing collaboration between data managers and statisticians — to ensure appropriate management of critical variables — is crucial to study success. It was even 20% less expensive with Cytel."

- Dr. Patrice Rioux, Chief Medical Officer, Raptor Pharmaceuticals

Cytel

One Stop: Advanced Trial Design, Data Analytics and Medical Writing

Assessments

- Responding to the FDA's SPA, Raptor and Cytel counterparts assess how the trial design changes will affect other study aspects crucial for success
- The sponsor realizes that to optimize both the operational performance and NDA filing process, the trial design, data handling, statistical analysis, and report writing are best managed in parallel, with the respective teams collaborating closely
- Raptor could achieve significant savings by also using Cytel for the data-related services

Responses

- Using simulation techniques, Cytel designed a non-inferiority trial with unblinded sample size re-estimation (SSR) at an interim analysis
- The adaptive approached was acceptable to both the FDA and the EMA
- Cytel was awarded biostatistics and statistical programming, followed by data migration and report writing services
- Raptor relied on Cytel programmers and medical writers to prepare the data from six studies for regulatory submission
- Cytel's CDISC Implementation Team developed SDTM and ADaM data sets compliant with the requisite guidelines

Outcomes

- FDA and EMA submissions were filed as scheduled in 2012, leading to FDA approval of PROCYSBI within a year
- PROCYSBI's FDA approval triggered a second $25 million payment per a development agreement with HealthCare Royalty Partners
- By partnering with Cytel, Raptor reduced costs by 20% and was confident that the essential components for a successful program were thoroughly synchronized
- Raptor has brought EDC development, clinical data management, and biostatistics under one roof with Cytel for their new Phase 3 studies

Preparing for NDA Submission

In addition to the adaptive trial design, Cytel experts handle for Raptor:

- CDISC CRF Annotation
- CDISC Migration
- ADaM Development
- ISS/ISE SAP & Programming
- Define XML and PDFs
- CSR and ISS/ISE Medical Writing

Cytel Clinical Research Services

At Cytel we believe the clinical development of drugs, biologics and devices is crucial for human welfare. Our mission is to improve success rates in this endeavor. We do this by improving the design and implementation of clinical trials, often employing adaptive approaches. Every Cytel-designed adaptive trial examined by FDA reviewers has been deemed acceptable.

All the major pharmaceutical, biotech and medical device companies are our customers. We also count among our customers and research partners leading academic, medical research institutions, and regulatory agencies worldwide.