CERTARA

Rare Disease and Orphan Drug Development

Unique Challenges Require Unique Approaches to Development

Developing drugs for rare diseases poses a range of clinical, regulatory, and commercial challenges. Small patient populations and limited research on orphan diseases make it difficult to set clinical endpoint, biomarkers, and outcomes measures. Sensitive patient subpopulations ranging from neonates and pediatrics to adults with co-morbidities make conducting clinical trials ethically problematic.

Certara is the global leader in model-informed drug development and has supported more rare and orphan R&D programs than any other consultancy. Our expertise in clinical pharmacology strategy and modeling and simulation (M&S) services enable us to quantify drug-disease-trial and exposure-response models from small patient populations providing insights into biomarkers and endpoints.

Using quantitative approaches, Certara informs trial design, dose selection and dosing regimen, identifying drug-drug and drug-food interactions along with other safety factors to optimize conditions for drug use. We can also model the impact of a drug in development on other disease states or untested populations. These proven quantitative methods are actively encouraged by global regulators who have demonstrated extraordinary flexibility in approving orphan drugs either through an accelerated approval pathway, the elimination of a second pivotal clinical trial, or applying M&S in lieu of certain trials.

Spearheading the Regulatory Process

Certara is a differentiated scientific leader within this challenging field combining technology and the regulatory and commercial expertise that comes from partnering with dozens of rare disease developers. Early and careful planning is critical for rare disease development and Certara's hundreds of PhD quantitative and regulatory scientists provide expert guidance and active support from pre-IND meetings through clinical development and post-market approval. Our regulatory writing and operations team of 200 professionals is experienced in orphan, pediatric, oncology, and global filings and have the proven skill to articulate the value of the drug to regulators and payers.

Value Evidence and Market Access

Increased pricing pressure and competition for orphan drugs have impacted how payers and HTAs evaluate these new therapies. The sponsor's burden to demonstrate value not only for competitive products but also for products with no therapeutic alternatives has been impacted by the doubling of new rare disease approvals, high prices, restricted access and overall budgetary impact. Certara develops a quantitative Multicriteria-decision analysis-based framework adapted to the very specific issues in rare disease development and access including quality of evidence, disease severity, ethical considerations, population-level factors, economic impact of the disease, and specific budgetary impact. By combining disease information, patient input, real world data, and innovative pricing and contracting strategies with the wider social and health benefits, we build robust, evidence-based results to justify market access and pricing.

Focus on Pediatrics

Regulatory agencies worldwide encourage M&S to "get the dose right." M&S reduces risk in pediatric product development—from translational science through clinical trial design, formulation development, and post-marketing. Certara scientists leverage sparse data and pre-clinical study, adult trials, literature data, and pediatric studies of related indications or drug actions to inform models of patient physiology, drug actions, and trial characteristics. Certara works closely with clients to harness M&S outputs to develop and iterate clinical trial design, explore alternative dosing scenarios, *in silico* patient responses, drug-drug interactions, and whole trial outcomes.

Certara can support PIP/PSP development plans with PopPK(PD) models that integrate a range of maturation and disease factors with allometric scaling to set the best dose for the first pediatric trial cohorts. This "learn and apply" approach is repeated for each cohort with additional M&S used throughout the cycle. Certara scientists can also leverage the Simcyp Pediatric Simulator, the industry's most sophisticated PBPK technology for modeling drug performance in neonates, infants, and children.

Unparalleled Experience in Orphan Drug Development

Certara has partnered with biopharmaceutical companies of all sizes on drug development plans for a wide range of rare/orphan diseases.

Genetic & Hereditary

- Fabry Disease
- Pompe Disease
- Hunter's Disease
- Metachromatic Leukodystrophy Disease
- Transthyretin-mediated Amyloidosis
- Urea Cycle Disorder
- Hereditary Anglodema
- ACE-induced HAE
- Lennox-Gastaut Syndrome
- Familiar Mediterranean Fever
- Gaucher Disease
- Cystic Fibrosis
- Hypophosphatasia
- Chronic Liver Disease
- Huntington's Disease
- Dravet Syndrome
- Thrombocytopenia
- Hereditary Transthyretin-mediated Amyloidosis

Antinfectives/Antivirals

- Anthrax
- Orthopoxvirus/Smallpox
- Symptomatic Botulism
- Respiratory Syncytial Virus

Gastrointestinal

- Short Bowel Syndrome
- Pediatric Crohn's Disease
- Carcinoid Syndrome

Oncology

- Acute Lymphoblastic Leukemia
- Metastatic Myeloma
- Multiple Myeloma
- Acute Myeloid Leukemia
- Urinary Bladder Cancer (Photodynamic Therapy)
- BRAF Mutation
- Blood Cancer
- Ovarian Cancer

CNS

- Myasthenia Gravis
- Restless Leg Syndrome
- Spasticity due to Multiple Sclerosis
- PKAN (Pantothenate Kinase-associated Neurodegeneration)
- Friedreich's Ataxia

Blood Disorders

- Paroxysmal Nocturnal Hemoglobinuria
- Atypical Haemolytic Uremic Syndrome (aHUS)
- Beta-thalassemia (Sickle Cell Beta-thalassemia)

Bone & Muscle Disease

- X-linked Hypophosphatemia
- Duchenne Muscular Dystrophy
- Hypophosphatasia

Other

- Radiation Poisoning
- Hypoparathyroidism
- Molybdenum Deficiency
- Peyronie's Disease
- Hyperuricemia in Patients with Gout Refractory
- Hepatic Veno-occlusive Disease
- Onchocerciasis

About Certara

Certara enables superior drug development and patient care decision-making through model-informed drug development, regulatory science, real-world evidence solutions and knowledge integration. As a result, it optimizes R&D productivity, commercial value and patient outcomes. Its clients include hundreds of global biopharmaceutical companies, leading academic institutions, and key regulatory agencies across 60 countries.

For more information visit www.certara.com or email sales@certara.com.

BR Oct 2018 v1 101618