ABSTRACT

Both registry studies and natural history studies play important roles in rare disease research. Understanding the differences between the two types of studies and how they can be used to inform clinical development can help sponsors plan for success.
Introduction
Sound drug development requires a comprehensive understanding of the disease being treated. To design reliable clinical studies and achieve meaningful outcome measures, researchers must apply known etiology and thorough knowledge of the disease’s progression. For rare diseases, this information is often minimal at best: patient numbers are small and historical data is spread across treating physicians who operate around the world.

It is essential for sponsors, patient advocates, and other stakeholders to use data on the natural history of these diseases to drive discussion and formulate drug development strategy. There are two prevalent data collection approaches:

1. Registry studies, which may include broad collection of defined data
2. Natural history studies, which are used for controlled, detailed collection of data that is subject to regulatory scrutiny

While registry and natural history studies both play important roles in rare disease research, it is important for sponsors to understand the differences between the two types of studies and how they can be used. In this white paper, we explore the differences between registry and natural history studies, as well as how to design and execute a natural history study to successfully support drug development.
Pathway to development in rare diseases

Similar to common diseases, drug development in rare disease research begins with building a strong base of knowledge about the disease to be treated. This beginning is followed by a focus on the therapeutic itself – understanding the investigative product’s proposed mechanism of action, obtaining assurance of consistency in product quality, and manufacturing and leveraging pharmacology toxicology data to support the clinical program. The next step in the pathway is design and execution of clinical studies to establish safety and efficacy primary endpoints and assess the benefit-to-risk ratio.

However, in rare disease, both disease information and the data needed to support the later steps of development is very limited, creating the need for registry or natural history studies.

Factors that have an impact on our knowledge of rare diseases – and the subsequent development of therapeutics – include:

+ Scarce and incomplete data about the disease
+ Small populations
+ Heterogeneity of the disorders
+ Lack of precedents for drug development
+ Necessity for more (and more careful) planning

The role of registries and natural history studies in rare disease research

There are two main types of clinical studies – interventional studies (or, clinical trials) and observational studies. In a clinical trial, participants receive specific interventions according to the protocol to try to determine the objectives of the study. On the other hand, in an observational study, participants may receive diagnostic, therapeutic, or other types of interventions, but the protocol does not assign participants to a specific intervention.

While the distinctions between these two types of studies appear straightforward, the definitions for observation studies are not harmonized worldwide. For example, regarding observational studies, EU Directive 2001/20/EC adds that no additional diagnostic or monitoring procedures shall be applied to the patients. However, the EudraLex Volume 9A provides clarification that interviews, questionnaires, and blood sampling may be considered as normal clinical practice.

Often, the terms registry study and natural history study are used interchangeably, but they are not the same, and it is important to understand the differences.

Definition and role of patient registries

A patient registry is an organized system for the collection, storage, retrieval, analysis, and dissemination of information on individual persons who have one of the following:

+ A particular disease
+ A condition (or, a risk factor) that predisposes them to the occurrence of a health-related event
+ Prior exposure to substances known or suspected to cause adverse health effects

A patient registry may include purpose-driven collection of demographic, epidemiological, clinical-effectiveness, cost-effectiveness, quality-of-care, quality-of-life, and care-pattern data. However, patient registries are generally unrestricted in their goals and can be set up to collect any set of data. They are typically less structured and controlled, and may even include patient communications and post-marketing data.
The purpose of patient registries is broad in scope and can be defined as needed, making registry studies applicable across the full spectrum of the drug development pathway. Patient registries can play a role in:

+ Collecting disease information
+ Advancing research hypotheses
+ Recruiting patients for clinical trials
+ Observing population behavior patterns
+ Monitoring health care and outcomes
+ Studying best practices in care or treatment

While patient registries can support a variety of applications, it is important that registry studies are set up and executed in such a way that data will be useful and compatible with the registry itself.

**Definition and role of natural history studies**

A natural history study documents the natural course of a disease from the time immediately prior to its inception and progressing through its presymptomatic phase and different clinical stages to the point where it has ended and the patient is either cured, chronically disabled, or dead without external intervention.

Unlike patient registries, natural history studies are very specific in their intention. Natural history studies can be useful for:

+ Tracking the course of a disease over time
+ Identifying variables that correlate with the disease and outcomes in the absence of treatment. These may include demographic, genetic, environmental, or other factors.

+ **Informing drug development and assisting with clinical trial design.** Information derived from natural history studies can help define the disease and identify gaps. Natural history studies can also be used to:
  - Obtain better estimates of prevalence
  - Identify and evaluate potential biomarkers
  - Evaluate potential clinical outcome assessments
  - Determine feasibility of a specific battery of assessments

In select situations, a natural history study can be used to represent the control population, if it is designed to meet the current regulatory requirements for inclusion in a regulatory submission. In fact, natural history studies can be critically important in rare diseases, where populations are small and the inclusion of a control of placebo population is more likely to be limited.

**Regulatory considerations**

When criteria for an observational study are clearly met, the studies only require institutional review board (IRB) or Ethics Committee review. Review by a regulatory agency or competent authority is not required. However, there is a gray area in the delineation between observational and interventional studies when additional diagnostic interventions are included. In these situations, there is a need to ensure that the criteria for minimal risk is met. Minimal risk applies when the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life, or during the performance of routine physical or psychological examinations or tests. It is important to keep in mind that there may be differing interpretations of interventional versus non-interventional studies among EU member states.
Generally, the data gathered should be designed to inform interventional studies. Treatment approval does not depend on natural history data, and full Good Clinical Practice (GCP) documentation is usually not essential. Nevertheless, good quality is important, and some level of data and conduct quality assurance should be incorporated.

**Regulatory agency resources**

Both the U.S. Food and Drug Administration (FDA) and the European Medicines Agency (EMA) offer resources to guide sponsors in designing and conducting registry or natural history studies in rare disease.

**Industry resources**

There are also a growing number of industry resources available to educate and help standardize the design and conduct of these types of studies.

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**Figure 1. Agency resources**

<table>
<thead>
<tr>
<th>FDA</th>
<th>EMA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Meetings with the Office of Orphan Products Development</td>
<td>Sponsor’s Guide to an Orphan Designation</td>
</tr>
<tr>
<td>Rare Diseases: Common Issues in Drug Development</td>
<td>Guideline on Clinical Trials in Small Populations</td>
</tr>
</tbody>
</table>

**Figure 2. Industry resources**

- **Best Practices & Standardization**
  - EURORDIS-NORD-CORD Joint Declaration of 10 Key Principles for Rare Disease Patient Registries
  - Global Genes RARE Toolkits • Rare Disease Registries
  - European Platform for Rare Disease Registries (EPIRARE) • Deliverable D9.3 – Proposal for a Platform Set of Common Data Elements
  - NIH Office of Rare Disease Research • Common Data Elements

- **Funding Programs**
  - Orphan Products Natural History Grants Program
  - NORD-FDA Natural History Study Project
Case study: natural history study as historical control
Asfotase alfa is an enzyme replacement therapy indicated for the treatment of patients with perinatal/infantile- and juvenile-onset hypophosphatasia (HPP). This case study highlights the use of natural history data as a historical control, following detailed dialogue and an agreement with the FDA regarding study design and the use of retrospective data collected from two natural history cohorts.

Designing and operationalizing natural history studies
The objective of a natural history study is to gather enough data to truly understand the disease presentation and its progression, and then to identify opportunities to impact the disease. Key issues to consider when designing a natural history study include:

- Focusing the study on the disease, not the therapeutic
- Supporting the development of multiple therapeutic options
- Completing a natural history before clinical development begins
- Recognizing that a natural history study is most valuable for designing clinical trials and validating outcome measures and/or biomarkers
- Requiring good quality data, even if the study will not be included in regulatory submissions

Figure 3. Case study: asfotase alfa

Indication:
For the treatment of patients with perinatal/infantile- and juvenile-onset hypophosphatasia (HPP)

Orphan Drug Designation — 12 Sept 08
Fast Track Designation — 14 May 09
Breakthrough Designation — 21 May 13
• for the perinatal/infantile and juvenile forms of HPP
• BLA was reviewed as a Priority Review
• Included results of seven ongoing or completed clinical studies
• Including 2 critical clinical trials in perinatal/infantile form of HPP (n=68) and one in juvenile form of HPP (n=8)

The Division advised sponsor to establish a natural history cohort to be used as a comparator for efficacy analyses, and agreement was reached that the endpoints of overall survival and ventilator-free survival are acceptable for the perinatal/infantile HPP population. For the juvenile-onset form of HPP, although not formally agreed, a comparison to a natural history group was also seen as potentially acceptable.

Efficacy supported by comparison with data collected retrospectively from two natural history cohorts – one for the perinatal/infantile and one for the juvenile-onset HPP (n=48)
The objective of a natural history study is to gather enough data to truly understand the disease presentation and its progression, and then to identify opportunities to impact the disease.

**Types of natural history study designs**

There are several types of natural history study designs, each of which has advantages and disadvantages. The designs may be retrospective, focused on the present, or prospective.

**Figure 4. Types of natural history study designs**
The literature review is likely the easiest, least expensive way to begin clarifying the natural history of a disease, but is limited by lack of access to patient medical records, inability to capture missing data, and difficulty in standardization. In addition, literature reviews may not meet the objectives of the natural history study.

Retrospective chart reviews are also relatively inexpensive, but are more resource-intensive than literature reviews. Retrospective chart reviews have their limitations, as well, including the need to establish prospective rules about how to address missing data and the need to obtain informed consent.

Figure 5. Comparison of retrospective natural history study designs

<table>
<thead>
<tr>
<th>Description</th>
<th>Literature Review</th>
<th>Retrospective Chart Review</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pros</td>
<td>• Inexpensive</td>
<td>• Relatively inexpensive</td>
</tr>
<tr>
<td></td>
<td>• Minimal resources required</td>
<td>• Limited resources required</td>
</tr>
<tr>
<td>Cons</td>
<td>• Limited to what is reported in the literature only with no access to patient medical records</td>
<td>• Charts are clinical charts, not research, so may be missing data</td>
</tr>
<tr>
<td></td>
<td>• No way to capture missing data</td>
<td>• Requires prospective rules about how to address missing data</td>
</tr>
<tr>
<td></td>
<td>• Difficult to standardize types of data collected in various articles</td>
<td>• No way to correct or question data</td>
</tr>
<tr>
<td></td>
<td>• May not meet the objectives of the natural history study</td>
<td>• Data elements can vary from site to site and can vary over time</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Requires informed consent to perform chart review though study likely considered to be of minimal risk to patient</td>
</tr>
</tbody>
</table>
A prospective cross-sectional study collects data from a variety of patients at a particular point in time, while a prospective longitudinal study collects data from a variety of patients over a prospectively defined period of time.

**Figure 6. Comparison of prospective natural history study designs**

<table>
<thead>
<tr>
<th>Description</th>
<th>Prospective Cross-Sectional</th>
<th>Prospective Longitudinal</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Description</strong></td>
<td>Collection of data from a variety of patients at one point in time</td>
<td>Collection of data from a variety of patients over a prospectively defined period of time</td>
</tr>
<tr>
<td><strong>Pros</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Limited duration of study</td>
<td>• Predefined data elements</td>
</tr>
<tr>
<td></td>
<td>• Predefined data elements</td>
<td>• Able to assess disease progression over time</td>
</tr>
<tr>
<td></td>
<td>• May provide insight into generalities about disease</td>
<td></td>
</tr>
<tr>
<td><strong>Cons</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Doesn’t collect patient experience in time; data is a ‘snapshot’</td>
<td>• Can be quite lengthy to complete, especially in diseases that progress slowly</td>
</tr>
<tr>
<td></td>
<td>• Doesn’t provide robust data on the pace of the progression of a disease state</td>
<td>• Can be expensive</td>
</tr>
<tr>
<td></td>
<td>• Difficult to extrapolate from ‘snapshot’ to make assumptions about disease progression on a per-patient basis</td>
<td>• Need to plan for changes in measurements and SOC over time</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• May require amendments to adjust for additional assessments or biomarkers over time</td>
</tr>
</tbody>
</table>
Planning for a natural history study

As with any study, planning for a natural history study should start with careful consideration of the following:

+ What are the questions that the study is intended to answer?
+ Why types of questions are anticipated to be encountered during the clinical development of the therapeutic?
+ What data or data types will be needed to answer those questions?

To help maximize study success, it is also important to plan for change. In essence, a well-designed natural history study is an iterative process that requires a commitment to analyzing data early and frequently.

Using natural history studies to inform clinical development

There are a variety of ways in which natural history studies can inform the development of clinical trials.

To understand the disease presentation and progression. Understanding how the disease manifests itself and how it progresses can assist in determining the size and duration of a planned clinical trial, as well as inform endpoint selection and statistical considerations such as effect size. Questions that a natural history study might help answer include:

+ What are the major and minor manifestations of the disease?
+ What is the survival data as currently understood?
+ How does the disease affect physical and sensory function?
+ How does the disease affect neuropsychological functions?
+ What are the underlying genetics?
+ Are there distinct phenotypes? Can they be associated with specific genotypes or pathophysiologies?
+ How are the disease manifestations measured? Is there a need to further refine current instruments used to evaluate disease manifestation?

To understand the current standard of care (SOC) and its impact. Understanding the SOC for a condition and how it might vary over the course of the progression of the disease can inform patient selection, study endpoints, study duration, and inclusion/exclusion criteria. Questions that a natural history study might help answer include:

+ What is the SOC for the condition, including supportive care?
+ What are standard diagnostic practices associated with the disease?
How does the SOC change as the disease progresses (e.g., how does the SOC change from milestone to milestone in disease progression)?

What is the degree of variability in SOC based on various factors (e.g., geography or access to centers that provide specialized care versus no/limited access)?

How has the SOC changed over the course of the expected lifespan of likely participating patients?

What is the impact of the current SOC in terms of disease progression and survival?

To identify sensitive and meaningful endpoints for clinical trials. Determining which assessments most accurately reflect the progress of the disease is critical to selecting the appropriate clinical efficacy endpoints for future studies. Identifying potential measurements provides the opportunity to validate them prior to inclusion in a clinical trial. Questions that a natural history study might help answer include:

Which of the disease manifestations can be measured?

Which manifestations remain stable over time and for how long? Which ones fluctuate and over what period do they fluctuate?

Which manifestations progressively worsen over time?

Which methods of measurement are most appropriate to measure the manifestation in question? Are those methods validated? Do they accurately reflect all variations of the manifestation, or are they limited to certain stages or presentations of the disease?

Is the proposed endpoint appropriate to all patients, or only a subset of patients with the condition?

Would it be more appropriate to define new measurements for endpoints? If so, apply all of the questions above and define parameters for validation of any new measures developed.

To identify sensitive and meaningful biomarkers. Biomarkers can be very useful in clinical trials. In some cases, upon agreement with the regulatory agencies, biomarkers can be used as surrogate endpoints to demonstrate change in the disease state, or the impact of treatment. It is critical to ensure that any biomarker that is included in a primary or secondary endpoint is well-characterized and that biomarkers are validated before the start of clinical trials whenever possible. Questions that a natural history study might help answer include:

Which of the disease manifestations can be measured or characterized via a biomarker?

Do potential biomarkers correlate with disease manifestation, or do they correlate with the anticipated mechanism of action of potential therapeutics?

Does the biomarker correlate with a surrogate endpoint that can be used to characterize a clinical benefit?

Is the biomarker something that can be readily tested in most labs, or will a special assay have to be developed and validated to be able to use it in a clinical trial?
Operational considerations

There are various models for collecting data in a natural history study. Data collection can be performed through either local sites or central site(s).

**Figure 8. Local sites vs. central site(s)**

<table>
<thead>
<tr>
<th>Description</th>
<th>Local Sites</th>
<th>Central Site(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Data is collected by each patient’s individual HCP and submitted to central data collection</td>
<td>All assessments are performed at a limited number of highly experienced central site(s)</td>
<td></td>
</tr>
</tbody>
</table>

| Pros         | | Pros | |
|--------------| | Increased consistency among records and assessments | Sites develop expertise in protocol performance reducing potential for missed data or protocol violations |
| • Patients retain own HCP | | • Increased consistency among records and assessments | Sites develop expertise in protocol performance reducing potential for missed data or protocol violations |
| • Convenient for patients (limited travel) | | • Increased consistency among records and assessments | Sites develop expertise in protocol performance reducing potential for missed data or protocol violations |

<table>
<thead>
<tr>
<th>Cons</th>
<th>Cons</th>
<th>Cons</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>• Variability among multiple sites</td>
<td>• Requires patient travel</td>
<td>• Variability among HCPs visiting patients in their homes</td>
<td></td>
</tr>
<tr>
<td>• Sites may introduce inconsistencies in data due to small number of patients and lack of opportunity for repetition or application of learnings</td>
<td>• May result in more patients who drop out</td>
<td>• Requires significant training of a number of in-home providers for the duration of the trial</td>
<td></td>
</tr>
</tbody>
</table>

A combination model uses local sites to collect routine data and central site(s) to perform complex assessments. And, finally, in a patient-reported model, all assessments and data collection are performed in the patient’s home. The pros and cons of each model should be considered in the context of overall study objectives.

**Figure 9. Combination model vs. patient-reported model**

<table>
<thead>
<tr>
<th>Description</th>
<th>Combination Model</th>
<th>Patient Reported</th>
</tr>
</thead>
<tbody>
<tr>
<td>More common assessments performed by local sites with complex assessments performed at central site(s)</td>
<td>All assessments and data collection performed in patient home</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Pros</th>
<th>Pros</th>
<th>Pros</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>• Increased consistency with regard to complex assessments</td>
<td>• Extremely convenient for the patient, encouraging retention</td>
<td>• Increased consistency with regard to complex assessments</td>
<td>• Extremely convenient for the patient, encouraging retention</td>
</tr>
<tr>
<td>• Fewer visits that require patient travel</td>
<td></td>
<td>• Increased consistency with regard to complex assessments</td>
<td>• Extremely convenient for the patient, encouraging retention</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Cons</th>
<th>Cons</th>
<th>Cons</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>• Patients retain relationship with personal HCP</td>
<td>• Variability among HCPs visiting patients in their homes</td>
<td>• Patients retain relationship with personal HCP</td>
<td>• Variability among HCPs visiting patients in their homes</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Requires significant training of a number of in-home providers for the duration of the trial</td>
<td>• Requires significant training of a number of in-home providers for the duration of the trial</td>
</tr>
</tbody>
</table>
Applying Quality by Design to the Rare Disease Population: Special Considerations

Natural history studies require the cooperation and coordination of a variety of stakeholders, including industry, patients and advocates, investigators, and government agencies.

**Other considerations**

**Quality.** Quality should be considered at every stage of a natural history, from protocol design to definition of the monitoring strategy.

**Timing.** The optimal time for natural history studies is prior to undertaking clinical development of a therapeutic. As such, defining the natural history of the disease and validating endpoints/biomarkers should be complete before the start of clinical trials whenever possible.

**Using natural history data as control data** The use of natural history data as control data is appropriate only in select situations, and must be agreed upon with the relevant regulatory agencies even if all of the following criteria are met:

- Highly homogenous population or sub-group
- Evaluations are uniform across all sites and patients
- Evaluations are not easily influenced by variations in the SOC
- Data has been rigorously collected and verified/monitored

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Figure 10. Stakeholders in a natural history study

- **Industry**
  - Initiate NH activities as early as possible
  - Collaborate with other stakeholders to fund natural history studies

- **Government** (e.g., NIH, FDA)
  - Support NH studies even when no Rx target identified
  - Advise on NH study development

- **Patients and Advocates**
  - Patient identification
  - Research process education
  - Advisory role
  - Fundraising

- **Investigators**
  - Support patient participation
  - Data collection
  - Advisory role

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Registry and Natural History Studies
### Best practices

There are unique challenges associated with every aspect of a natural history study. An experienced contract research organization can help sponsors address those challenges with best practice solutions.

**Figure 11. Best practices for natural history studies**

<table>
<thead>
<tr>
<th>Project Area</th>
<th>Challenge</th>
<th>Solution</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Project Design</strong></td>
<td>• Understanding available and needed data</td>
<td>• Set realistic expectations</td>
</tr>
<tr>
<td></td>
<td>• Data variation between sites</td>
<td>• Identify the specific data points prior to study start</td>
</tr>
<tr>
<td></td>
<td>• Set realistic expectations</td>
<td>• Review sample patient charts, where applicable</td>
</tr>
<tr>
<td></td>
<td>• Identify the specific data points prior to study start</td>
<td>• Solicit CRF review from sites</td>
</tr>
<tr>
<td></td>
<td>• Review sample patient charts, where applicable</td>
<td>• Early listing review</td>
</tr>
<tr>
<td></td>
<td>• Review sample patient charts, where applicable</td>
<td>• Re-training as appropriate</td>
</tr>
<tr>
<td></td>
<td>• Solicit CRF review from sites</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Early listing review</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Re-training as appropriate</td>
<td></td>
</tr>
<tr>
<td><strong>Site Selection &amp; Management</strong></td>
<td>• Substantial time commitment needed</td>
<td>• Conduct site-level feasibility</td>
</tr>
<tr>
<td></td>
<td>• Limited resources at sites</td>
<td>• Develop site-specific plans</td>
</tr>
<tr>
<td></td>
<td>• Waning commitment</td>
<td>• Consider supplying resources</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Comprehensive communication</td>
</tr>
<tr>
<td><strong>Informed Consent</strong></td>
<td>• Conflicting requirements for ICF</td>
<td>• Solidify Sponsor requirements for ICF</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Identify local regulations and site-specific requirements</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Finalize the protocol in-line with requirements</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Select sites that can comply with defined requirements</td>
</tr>
<tr>
<td><strong>Data Management</strong></td>
<td>• Capturing historical data</td>
<td>• Design with options for unknown data</td>
</tr>
<tr>
<td></td>
<td>• Data strategy is subject to change after more and more data becomes available</td>
<td>• Ensure consistent review for all types of results</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Decide on standardized units and ranges early</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Standardize all labs</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Define what CRFs are required versus optional prior to data collection</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Define the scope of data cleaning</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Minimize queries</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Code concomitant medications and AEs</td>
</tr>
<tr>
<td><strong>Biostatistics</strong></td>
<td>• Unexpected data collected in database</td>
<td>• SAP: Allow some flexibility for the defined analyses</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Amend SAP if required</td>
</tr>
</tbody>
</table>
Conclusion

Natural history studies are resource-intensive studies that involve a number of stakeholders, all of whom cooperate to better characterize a rare disease. When executed properly, these studies can be very important to the design of clinical development of therapeutics for rare diseases. Thorough, thoughtful planning to the design and operational considerations of a natural history study will help ensure that the study design is well-defined, but also flexible to accommodate ongoing advances in treatment.
References

1. Lapteva L. Regulatory Applications for Products Intended to Treat Rare Disease.
Angi Robinson | Executive Director, Pediatrics and Rare Diseases
Angi Robinson has been studying rare diseases and pediatrics at Premier Research for over 15 years. She has provided oversight and management support for more than 30 rare disease studies in the U.S. and globally and has supported FDA pre-IND meetings, IND submissions, and NDA/BLA project directorship. Angi has worked on industry sponsored studies to support the approvals of four drugs with orphan drug designations. Her experience includes multiple study designs including natural history studies with retrospective and prospective designs as well as PK/PD, adaptive design, and FDA fast track and Breakthrough Therapy designations.

Ms. Robinson helped launch the first Best Pharmaceuticals for Children Act coordinating center, collaborating with leaders at the National Institute of Child Health and Human Development.

Ms. Robinson began her career in laboratory quality control and has worked in clinical trial management as a Project Director/Manager, Clinical Lead, and Clinical Monitor. She holds a bachelor’s degree in cell and molecular biology from Tulane University.

Juliet Moritz | Executive Director, Strategic Development, Rare Diseases
Juliet Moritz has worked in clinical research for more than 25 years, and her extensive background covers the spectrum from single-site studies to large, multinational trials. She joined Premier Research in 2016 to specialize in rare diseases, supporting the strategic development of products that address unmet medical needs associated with rare and orphan afflictions.

Prior to joining Premier Research, Ms. Moritz was Associate Director of Global Project Management at PPD Inc., overseeing infectious and respiratory disease research, and prior to that was Associate Director of Clinical Research at Knopp Biosciences. She held senior positions at Wyeth, Theravance, and PPD and began her career as a clinical research associate.

Ms. Moritz holds a Master of Public Health degree from the Drexel University School of Public Health and a bachelor’s degree in biology from the University of Pennsylvania. She is currently pursuing her doctorate in bioethics through Albany Medical College and in the process of completing the Stanford Professional Certificate in genetics and genomics.

About Premier Research
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