Pediatric Trial Design and Modeling: Moving into the Next Decade

Industry Approach to Innovative Pediatric Trial Design

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FDA Workshop

Great Room, US FDA White Oak

Industry Approach to Innovative Pediatric Trial Design

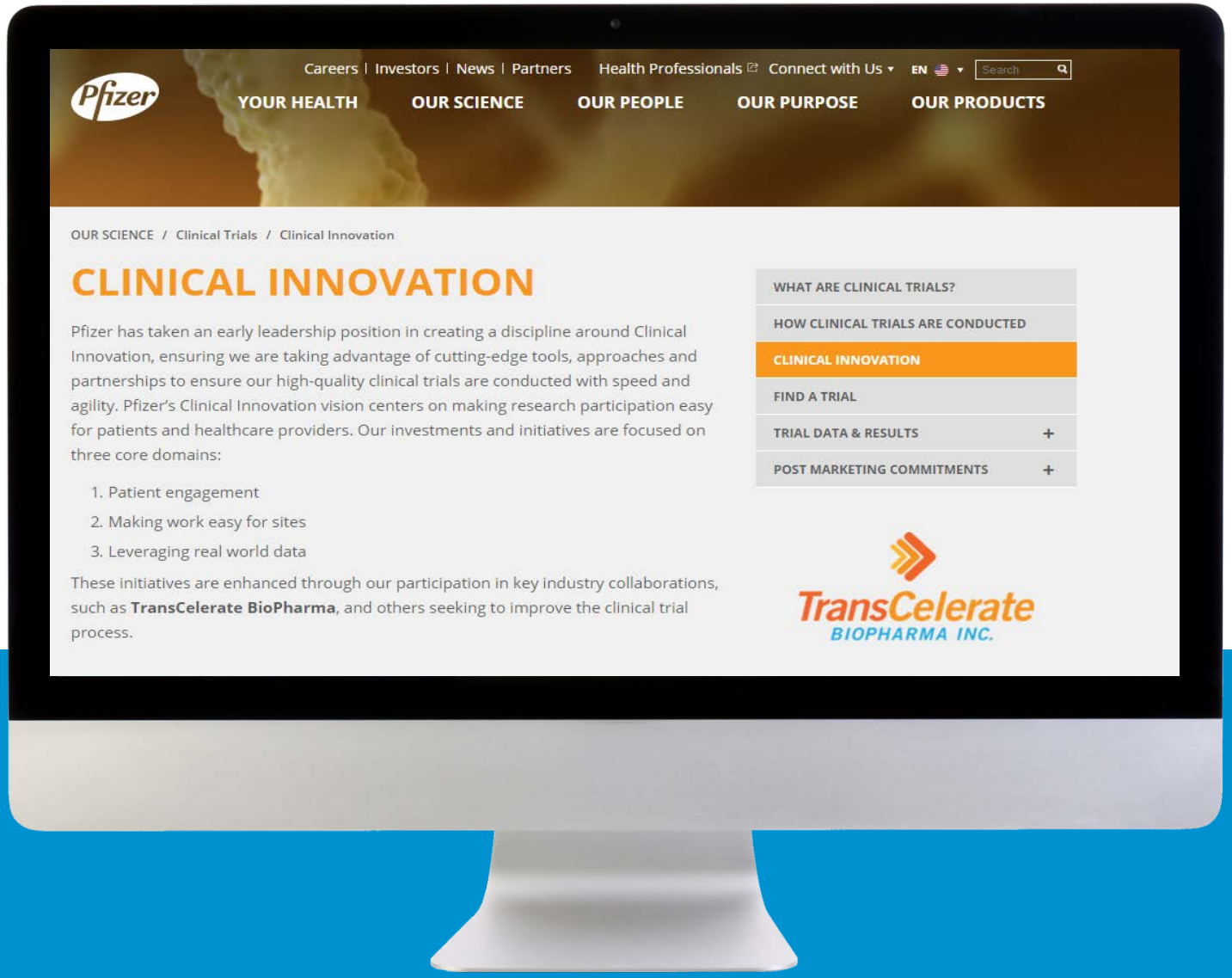
Agenda

What is Industry Doing to Improve Pediatric Clinical Trial Innovation

- Infrastructure
- Patient Engagement
- Collaboration

Innovative study design and solutions

Moving forward – call to action



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What is Industry Doing to Improve Pediatric Clinical Trial Innovation

Infrastructure

- Development of Pediatric Centers
- Support for pediatric age-appropriate trial design, study sites, study support and regulation
- Enhance Pediatric Education

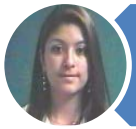
Pfizer Pediatric Center of Excellence (PedCoE)

Organization

Located in the Chief Medical Office of Dr. Freda Lewis-Hall

Mission Statement

To improve the health and well-being of children by applying science, driving operational excellence, aligning resources, and providing a unified voice for the needs of children



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Judy Skaggs, BS MSPM
- *Director, Pediatric Strategy & Operations*

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- *Global Lead, Pediatric Center of Excellence*

5 30-minute eLearning Programs

The Pfizer Pediatric Education series is a 5-module eLearning curriculum intended to educate colleagues and partners about key topics related to Pfizer policies and national and international regulations pertaining to Pediatric Drug Development.

The approximately 2.5 hour series includes input from over 25 Subject Matter Experts, both Pfizer colleagues and recognized industry leaders. Each 30-minute module targets specific roles, so most learners will not be required to complete all 2.5 hours.

	**Module 1:** Introduction to Pediatric Research at PFIZER	• Why Conduct Pediatric Trials • Challenges of Pediatric Clinical Trials • Pfizer Pediatric Research Resources • Pediatric Development Strategy & Timeline
	**Module 2:** Current Legislation and Regulatory Environment for Pediatric Research	• Prescribing Issues in Clinical Practice • More Medicines for Children: Legal/Regulatory Landscape • Why Is a Global Strategy Important? • Global Pediatric Strategies
	**Module 3:** Drug Development Considerations for Pediatric Research	• When to Start? • Getting the Drug In – Pediatric Formulations • Getting the Dose Right • Pharmacokinetics in Children
	**Module 4:** Designing a Pediatric Clinical Trial	• Pediatric Trial Considerations • Design Considerations • Designs for Pediatric Trials • Protocol Development
	**Module 5:** Pediatric Clinical Operations	• Plan for a Successful Trial • Site Identification and Recruitment • Operational Challenges of Limited Populations • Monitoring in Pediatric Trials

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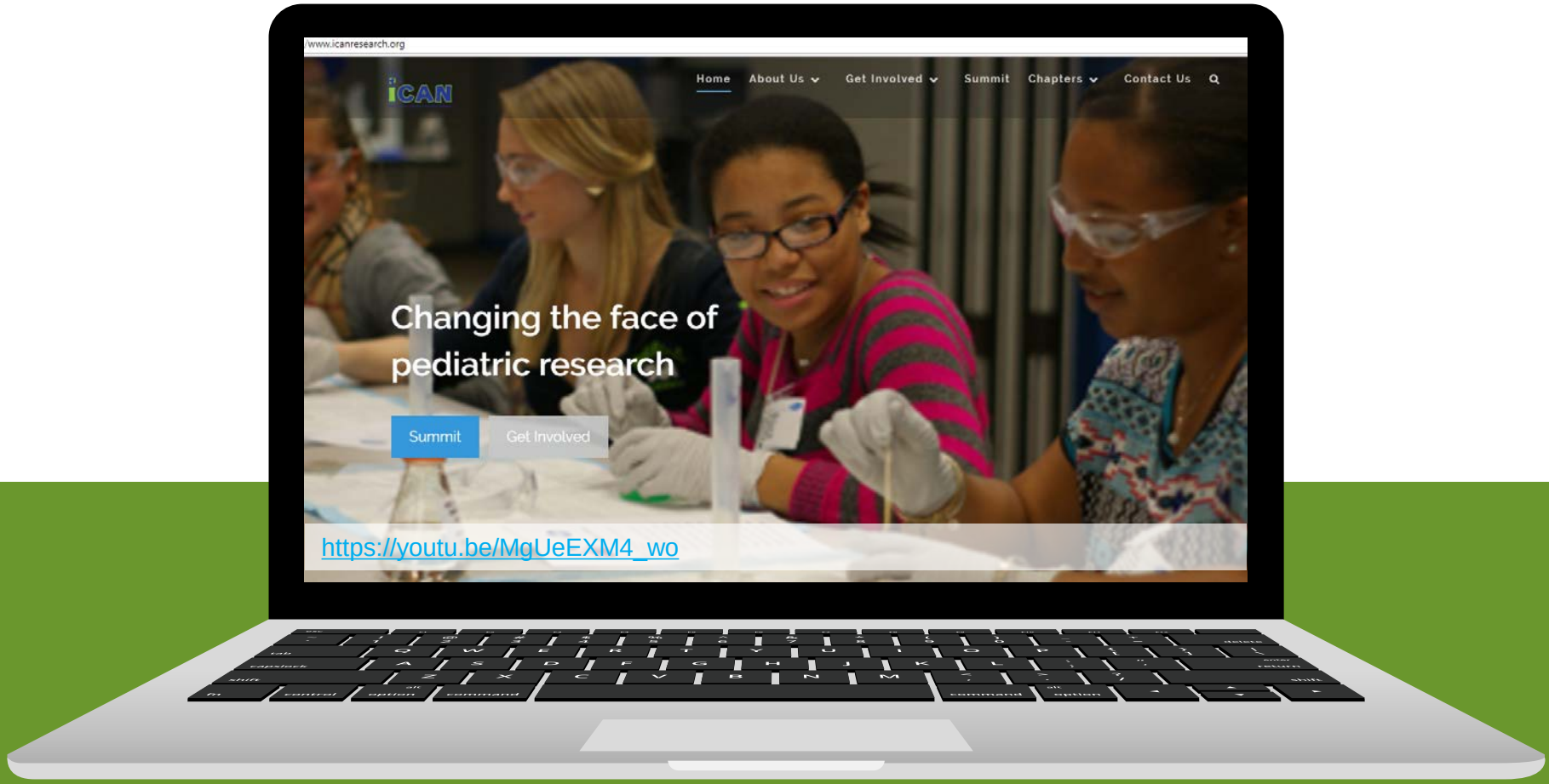
- Voice of child/caregiver (study design, simulation, feedback)

International Children's Advisory Network



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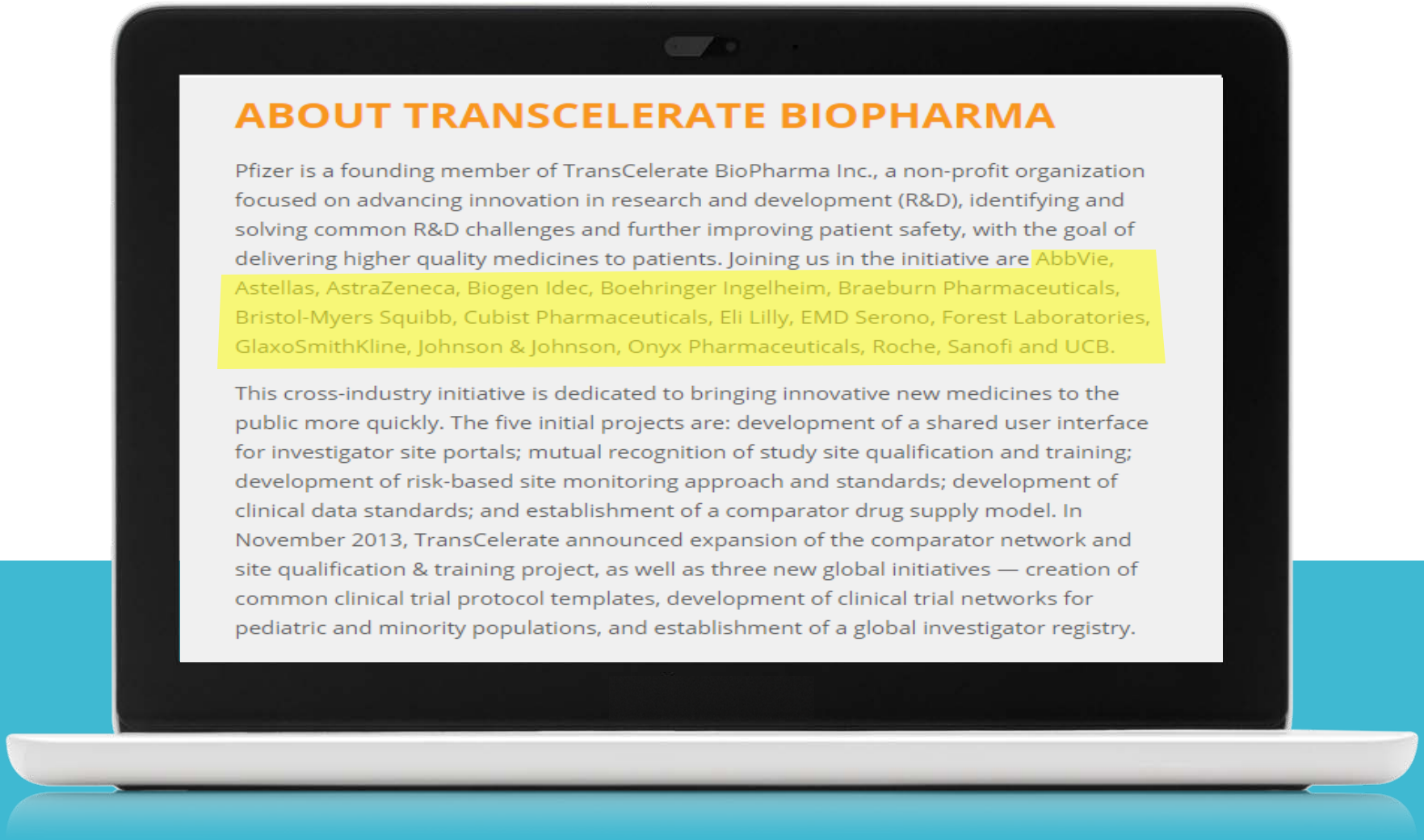
Collaboration

- Involvement with Collaborative groups (TransCelerate)
- Consortia
- Common protocol templates
- Study Design



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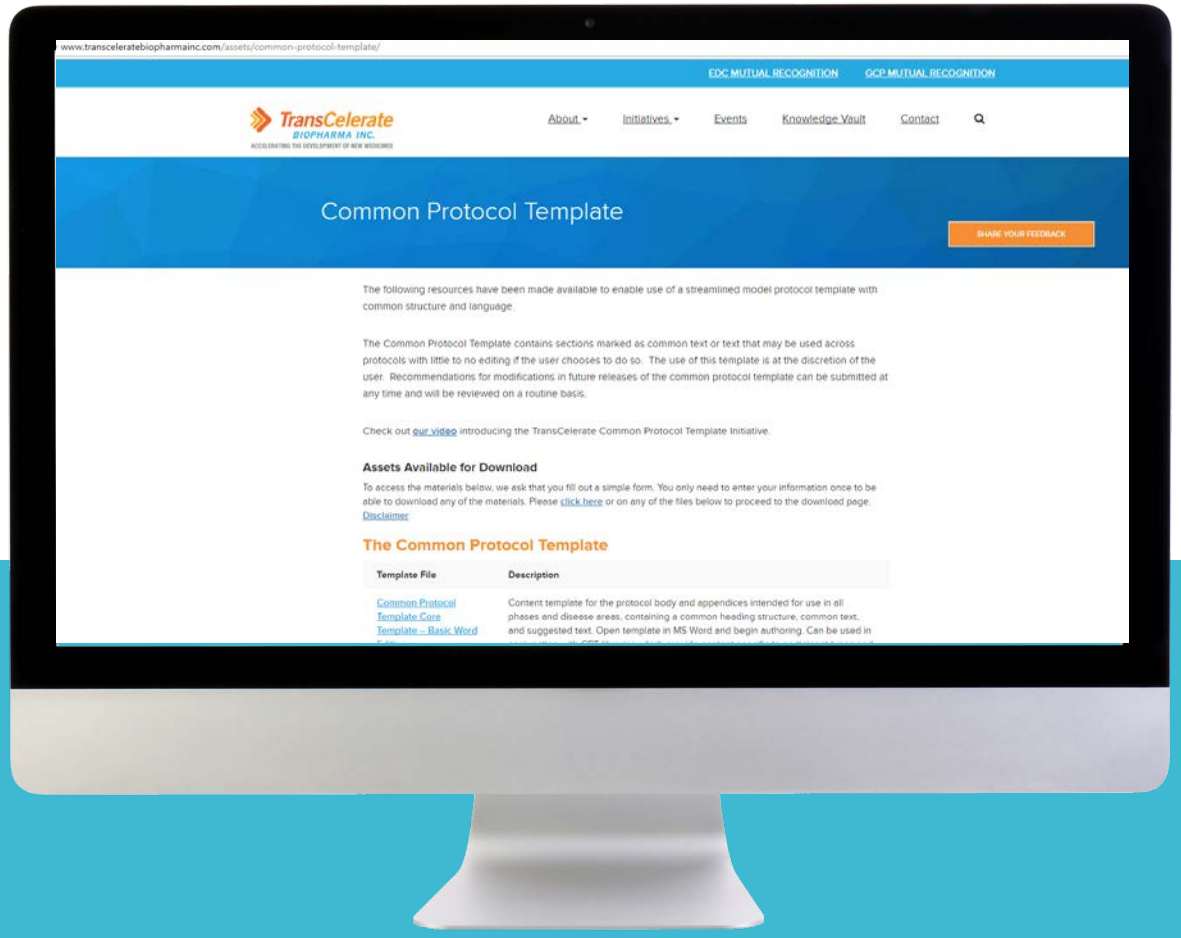
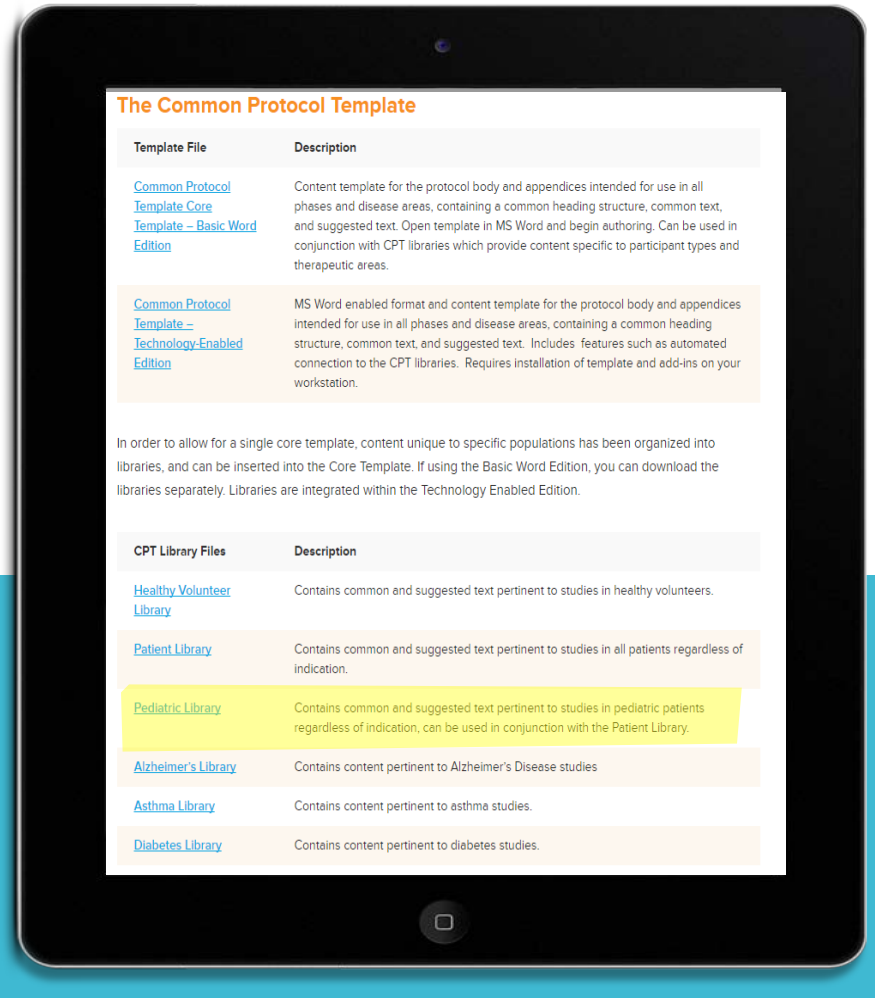
TransCelerate



TransCelerate Pediatric Protocol Template



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Examples of Innovative Methods to Inform Treatment of Children

- Extrapolation (including Modeling and Simulation)
- Adaptive design
- Real World Data/3rd party (published) data
- Protocol Simulation
- Sparse and scavenge sampling for PK
- Opportunistic studies

Leveraging Existing and Emerging Data… rather than Interventional Trials

Examples of Innovative Design/Solution

- **Background (anticoagulant):**
- 2 years ago – acquired from business deal peds study ongoing 8 yrs
- Rare condition; strict eligibility criteria; 5 cohorts of age groups (newborn, infant, pre-school, school age, teen);
- Over first 8 years – 5 amendments
- After first 6 yrs of enrollment – 23/50 patients enrolled (all but 2 in school age and up; no newborns or infants)
- CSR due Dec 2018

Examples of Innovative Design/Solution

- **Innovative Solution:**
- After transfer of study – type C meeting to broaden subject criteria; simplify protocol; add innovative design
  - Continue to enroll patients as agreed with FDA
  - Request use of individual subject data on neonates and infants from published studies (retrospective analysis; prospective IIR multicenter dose-finding study; prospective open label)
  - Totality of data projected available on FDA timeline

Examples of Innovative Design: Endpoint for Sickle Cell Disease Study

- Drug for prophylactic treatment of Vaso-occlusive pain crises (VOCs)
- Traditional endpoint - based on the number of in-patient hospitalizations (requires large sample size and lengthy trial)

  AND many patients avoid the hospital when possible for VOC treatment

Examples of Innovative Design: Endpoint for Sickle Cell Disease Study

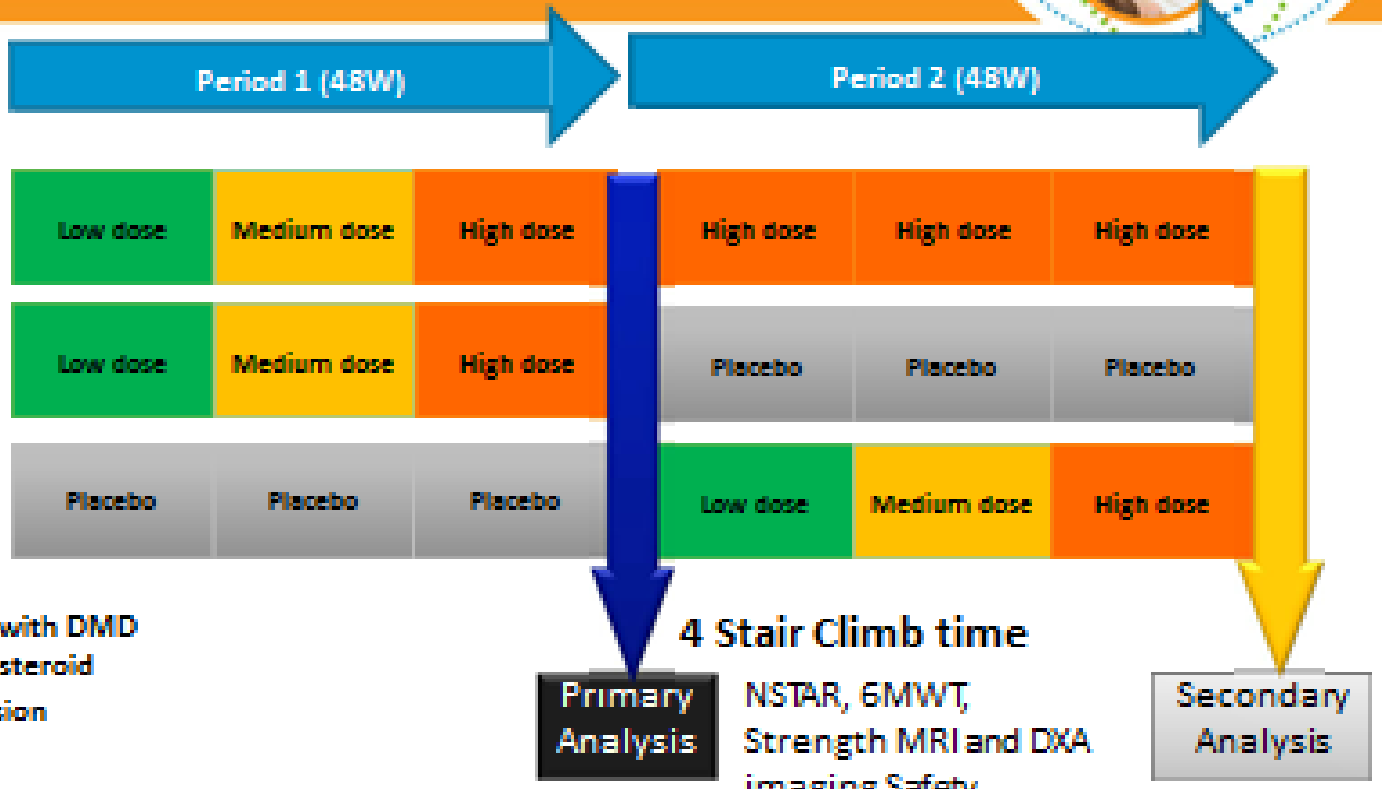
- Study team decided to describe the patient journey identify the concepts, and define a clinically meaningful endpoint model that reflects the painful crisis experience from the perspective of the patient to allow for the development of a validated endpoint for use in the clinical development program for the sickle cell disease treatment portfolio.

Examples of Innovative Design: Endpoint for Sickle Cell Disease Study

- End result – development different endpoint of the **“VOC day”** which allowed patients to record VOCs managed outside a hospital stay either at home or via out-patient treatment on an electronic patient report device (ePRO) similar to a cell phone.

Domagrozumab (PF-06252616):

Phase II Development in Duchenne Muscular Dystrophy (#NCT02310763)



- 6-<16 year old boys with DMD
  - Ambulant on steroid
- Monthly 2hr IV infusion
- Dose escelation
- N=35 Randomized per sequence (Total 105)
- Enrollment completed

External Data Monitoring Committee

Rare Disease
A Pfizer Research Unit

Examples of Innovative Design/Solution

Background (Fosphenytion)

1996 (21 years ago)	Post Marketing Commitment for pediatric study requested
1998	Pediatric supplement was summited
1999	Non-approval issued to supplement (identify dose that can produce levels of free phenytoin that are safe and effective in children
2001	FDA Written Request for 2 studies (PK and safety)
2010	FDA asked for IV phenytoin PK study in children
2011	Pfizer proposed a modeling and simulation (M&S) approach alternative + use of 3rd party data
2014	Received comments from FDA on M&S; focus on Cmax
2017	Completion

Take Home Message

Don't let PMCs linger for a long time

Don't hesitate to try a different approach

…in a collaborative manner with stakeholders

…and with appropriate scientific rigor

Persistence is often rewarded

Leverage well conducted studies from 3rd parties

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Industry Pediatric Study Design Challenges Call to Action

- Innovative study design vs traditional placebo controlled, interventional studies
- Inconsistences within the FDA divisions
- Old studies with long timelines
- Expertise in peds for all pediatric studies
- Are the studies feasible?
- Coordination between EMA and FDA