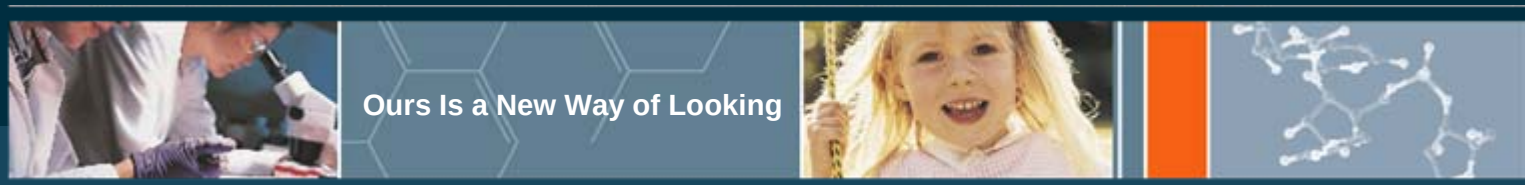
PTC Therapeutics, Inc.

Challenges in Developing Innovative Drugs Specifically For Rare Disorders

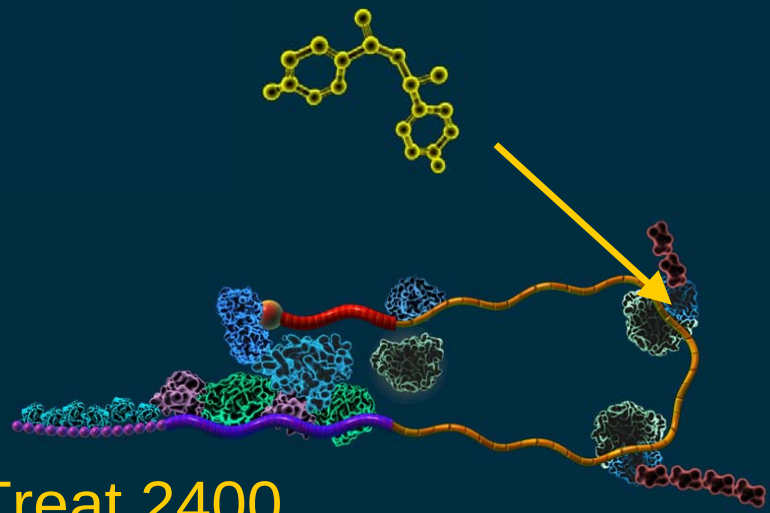


Stuart W. Peltz, Ph.D.
President and CEO

PTC Therapeutics, Inc.

- Biopharmaceutical firm established in 1998 out of Robert Wood Johnson Medical School
- Located in South Plainfield, NJ
- Currently ~170 employees
  - Biology, Chemistry, Pharmacology/Toxicology, Clinical, Commercial
- Focused on discovery and development of small-molecule drugs that modify **post-transcriptional control** (**PTC**) mechanisms
- Actively engaged in discovery and development of drugs for DMD, CF and other rare genetic disorders

PTC124



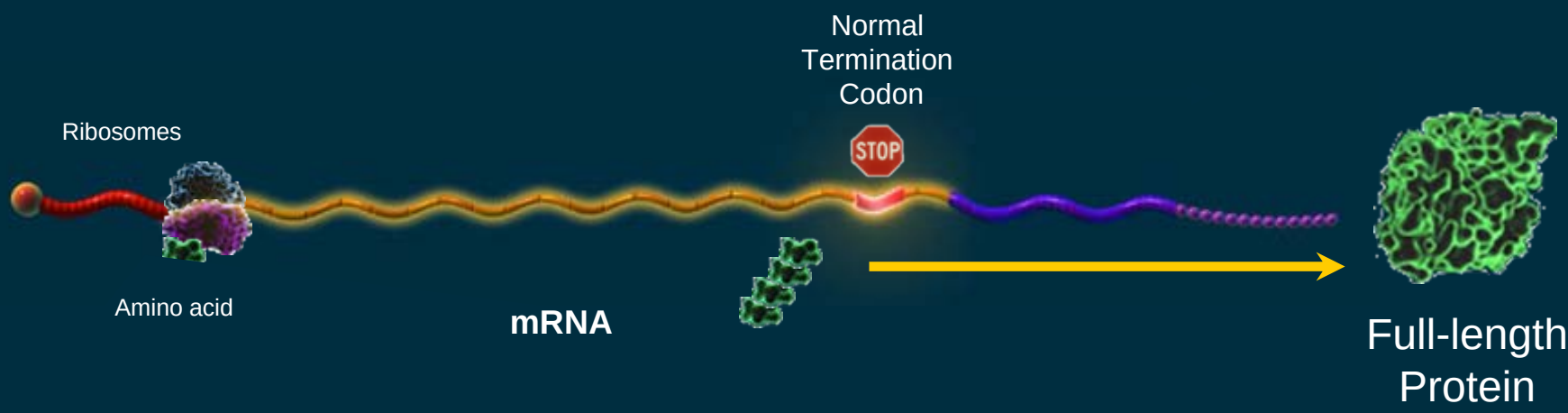
Example of Ultra-Orphan Drug Development: The Potential to Treat 2400 Distinct Genetic Disorders

Ours Is a New Way of Looking

PTC THERAPEUTICS

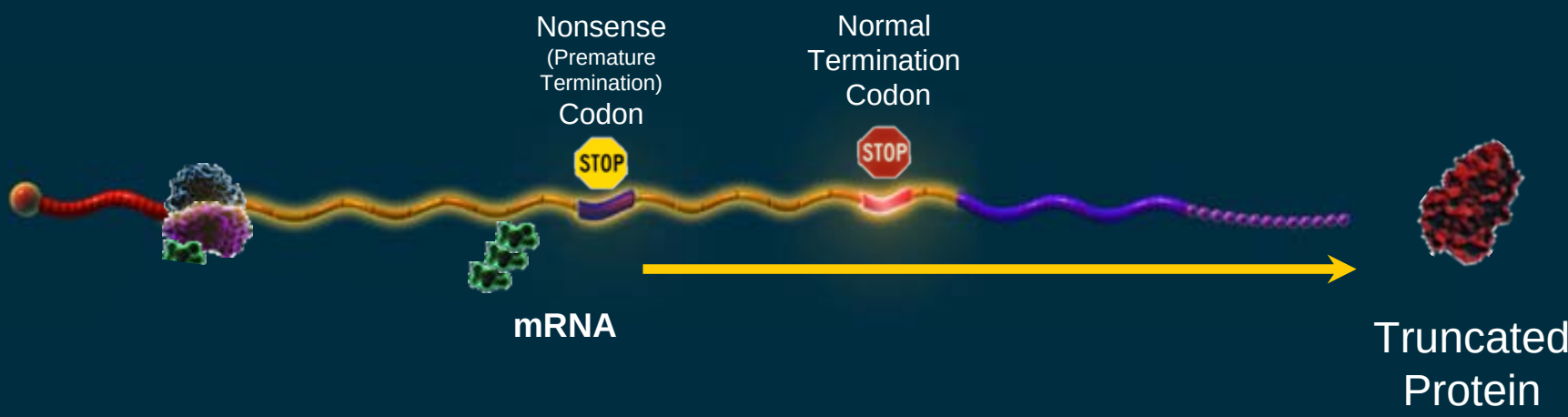
A Mechanism-Based Approach to Treating Genetic Disorders

Normal Translation



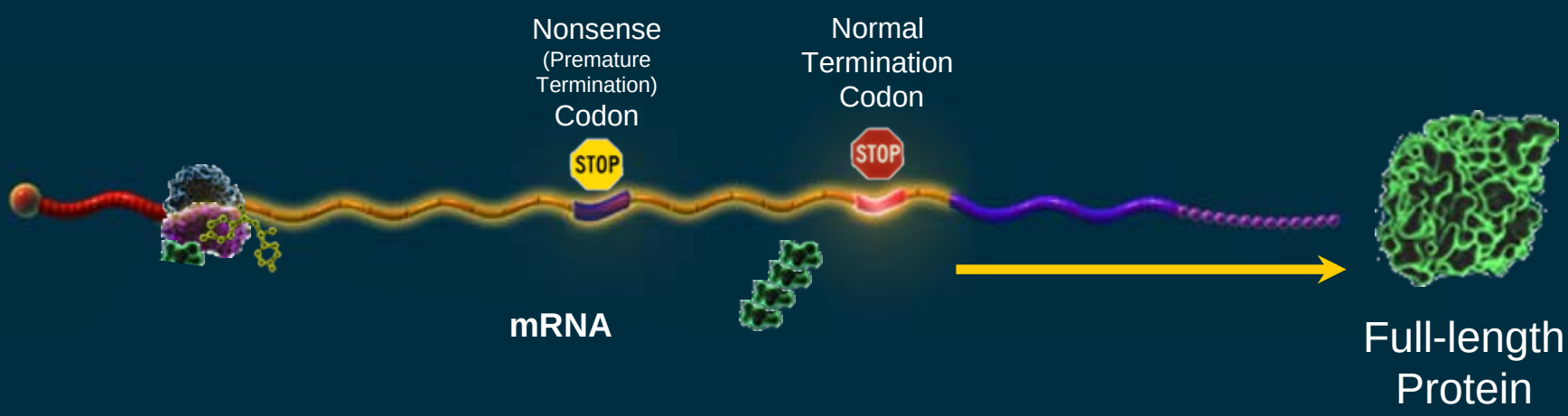
A Mechanism-Based Approach to Treating Genetic Disorders

Premature Termination



A Mechanism-Based Approach to Treating Genetic Disorders

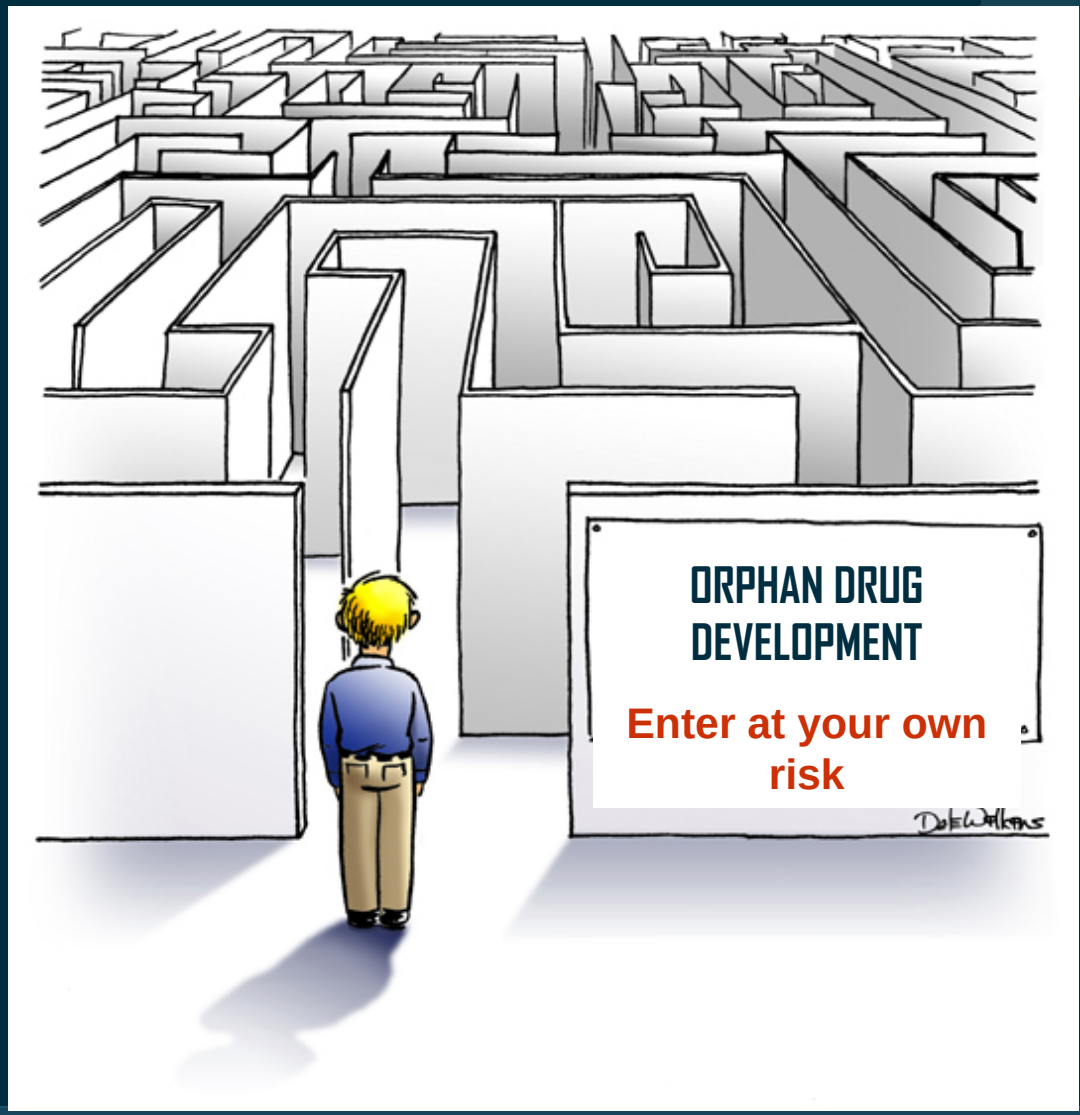
PTC124



2,400 Monogenetic Indications Have Been Identified

- The NIH Office of Rare Diseases estimates there are 6,000 rare diseases affecting 25 million patients in the USA
- NORD estimates that over 4,000 disorders can be considered genetic disorders with nonsense mutations as one of the likely causes
- Where characterized, the median percentage of patients with nonsense mutations is 15%

The Opportunity: How Do You Select The Potential Indications When There Are So Many?



R&D Challenges in Orphan Indications

Research/Preclinical

- Are there cell lines, animal models?
- Is there a established correlation of animal model data and human disorder/clinical endpoints?
- Is there an understanding of the epidemiology of the disorder: phenotypic and genetic subtypes, genetic differences?
- Are genotyping technology and resources available?

Clinical Trial Design

- What is the baseline disorder profile?
- What is the natural history of the disorder?
- What is the variability in outcome measures over time?
- What are potential regulatory clinical endpoints?
- Is the current information published or validated from a regulatory perspective?

Operational and Commercial Challenges in Orphan Indications

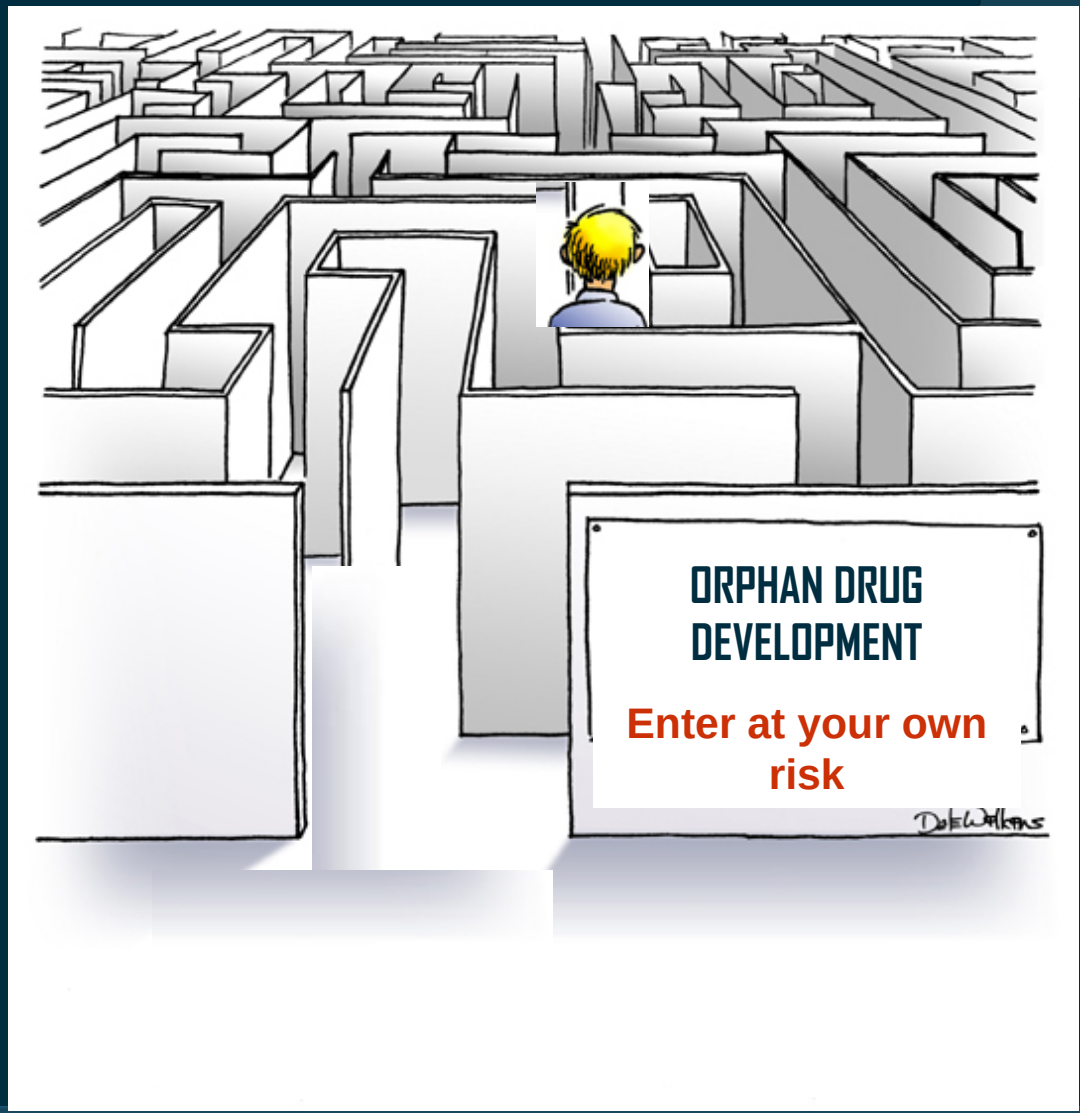
Operational

- Where are patients being diagnosed/treated?
- Which physician groups are involved?
- Are investigators experienced in clinical trials?
- Are there standards of care?

Pharmacoeconomic and Commercial

- What is the process and cost associated with diagnostics?
- What is the cost of the current treatment regimen?
- How could new drugs impact the course of the disorder in measurable outcomes (e.g., life expectancy, hospitalizations and other exacerbations)

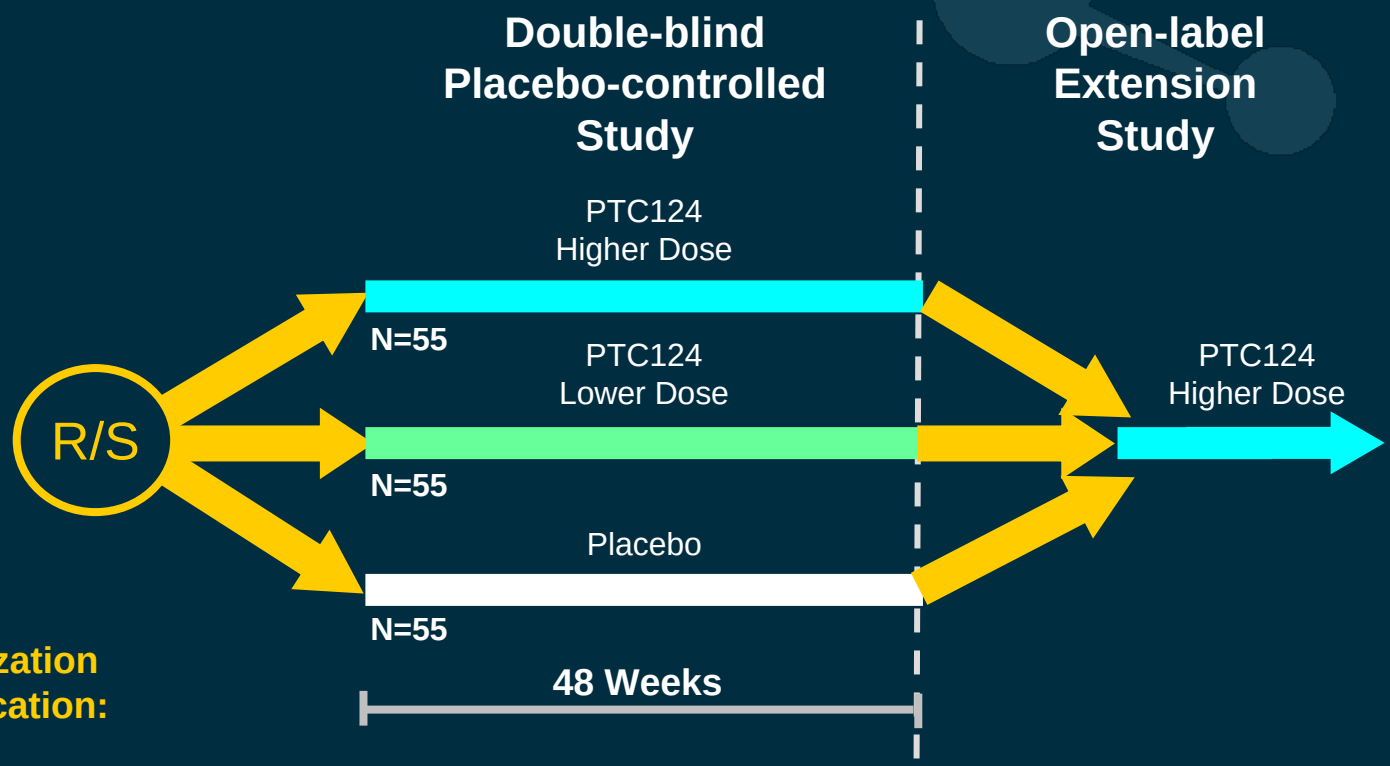
Our First Two Indications: Cystic Fibrosis and Duchenne Muscular Dystrophy



Initial Indications Cystic Fibrosis (CF) & Duchenne Muscular Dystrophy (DMD)

Characteristic	CF	DMD
Defined pathophysiology	Lack of CFTR Cl^- channel	Lack of dystrophin with impaired muscle integrity
Eligible patients world-wide (% nonsense mutations)	70,000 (10%)	25,000 (13%)
Life-threatening & disabling	~36-year median survival Severe lung dysfunction	~22-median survival Progressive muscle loss
High unmet need	Palliative therapies only	Serious steroid side effects
PD & clinical endpoints	TEPD, PFTs, cough, exacerbations	Muscle dystrophin, serum CK, ambulation, activity monitoring
Strong patient advocacy	CFF	MDA, PPMD, AFM
Nonsense mutation models	G542X mouse	*mdx* mouse

DMD Pivotal Study Design



Eligibility Criteria:
- Nonsense-mediated DMD
- Males, ≥5 years
- Ambulatory (can walk ≥75 meters)

Randomization & Stratification:
- Age
- Steroid use
- Baseline 6-minute walk distance
- Multiple 2º and 3º endpoints

Primary Outcome Measure
- 6-minute walk distance

DMD/BMD Phase 2b Study Site Locations

★ Site activated and able to enroll patients

★ Site level IRB/IEC submission completed

Estimated patient numbers by site: 3-12

Estimated total patient number: 101

DMD/BMD Phase 2b Study Site Initiations are

- ★ Site activated and able to enroll patients
- ★ Site level IRB/IEC submission completed

Estimated patient numbers by site: 3-8

Estimated total patient number: 88

Challenges For Ultra-Orphan Drug Development

- Small patient populations with high unmet medical need
  - Natural course of disease is not well understood
  - Limited standardization in diagnosis and treatment
  - Propensity to heavily loaded clinical trials to better understand condition and treatment
- Unmapped clinical path forward
  - Investigators often have limited experience in clinical trials
  - Burden on the sponsor to provide extensive training to all site personnel
  - Clinical endpoints need to be defined and validated
  - Tools and techniques for measurement need to be standardized
- Standard regulatory processes and protocols
  - Inefficient for orphan conditions
  - Insensitive to the time pressures of smaller enterprises
  - Federal review divisions not aligned with developments of genetic therapies

Encouraging Successful Development in Rare Disorders

- Global registry to identify study sites and appropriate patients
- Travel coordination/language translation for study sites outside of the US
- Consensus on disease course, diagnostic testing and treatment protocol
- Central IRBs to substantially speed up the review process and contract negotiations
- Regulatory sensitivity to the initial candidate in start-up enterprises

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