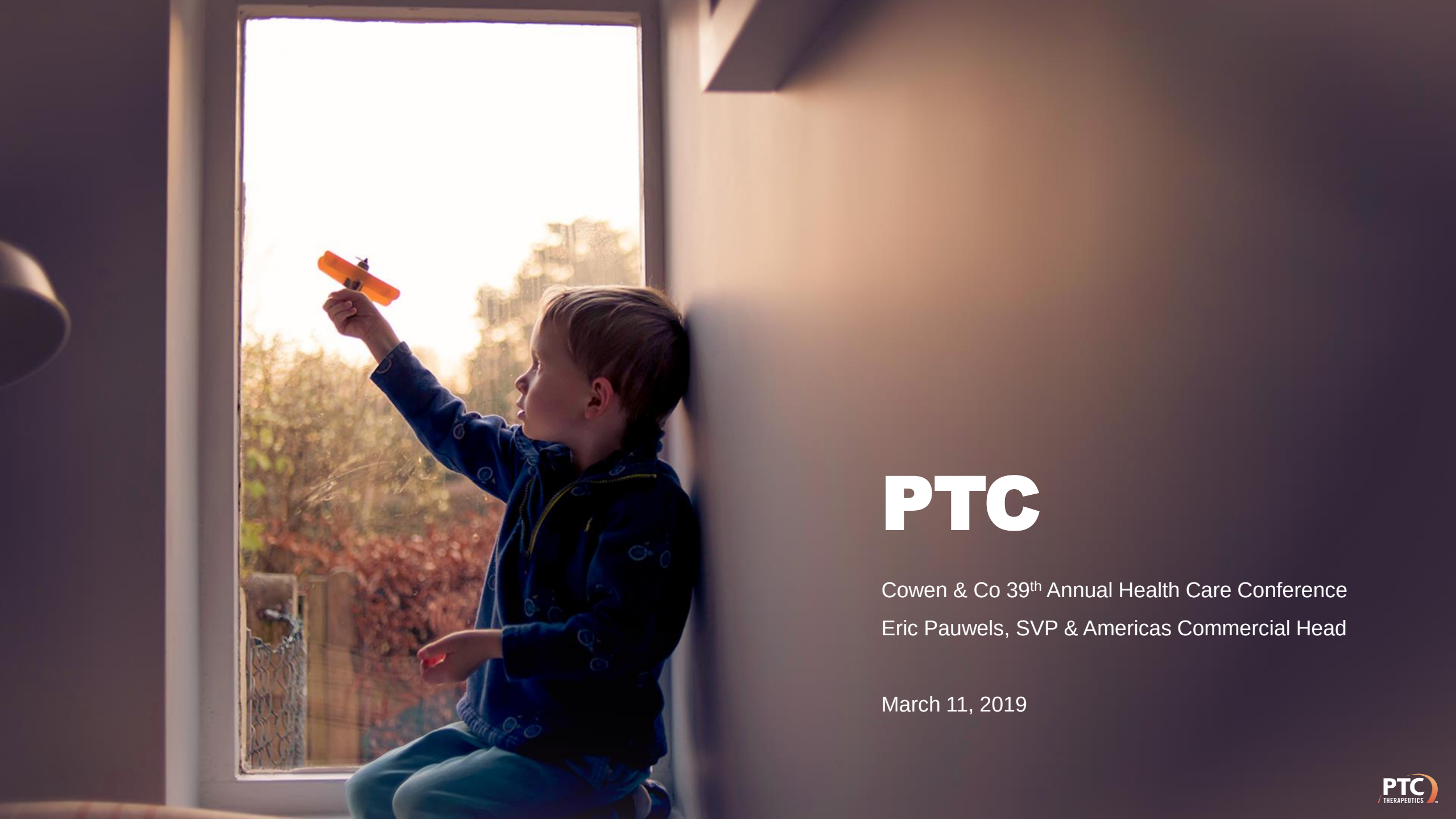


# PTC

Cowen & Co 39th Annual Health Care Conference

Eric Pauwels, SVP & Americas Commercial Head

March 11, 2019

# Forward looking statement

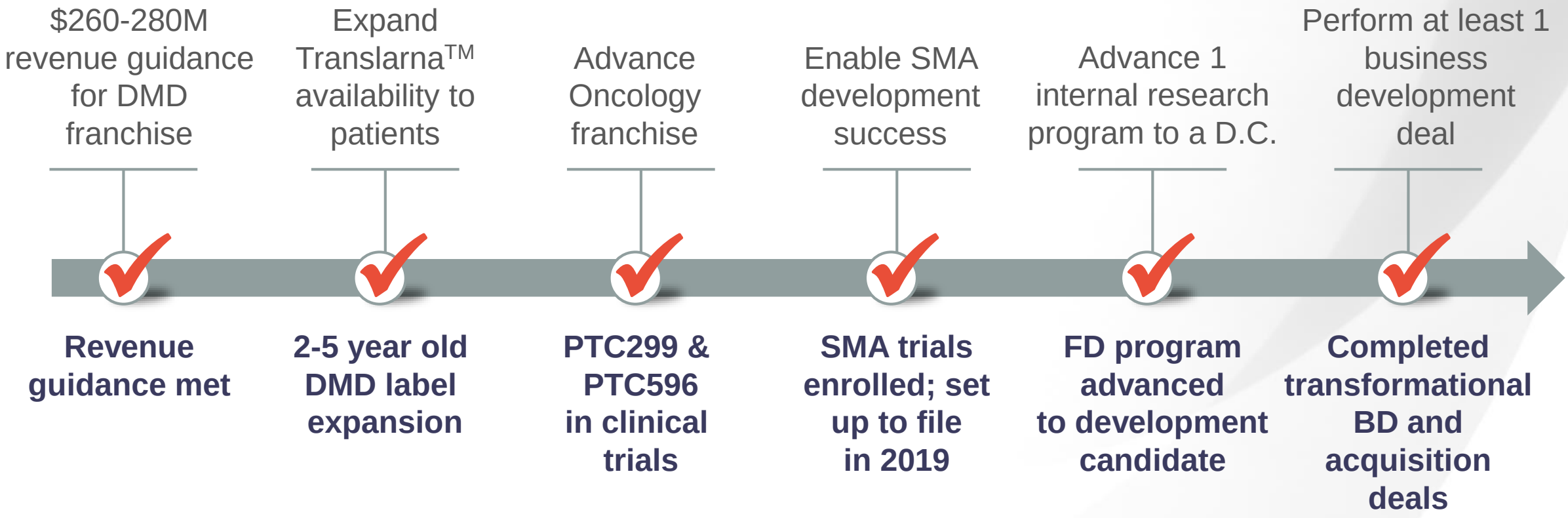
All statements contained in this presentation, other than statements of historic fact, are forward-looking statements, including statements related to preliminary unaudited 2018 financial information with respect to 2018 net product revenue of Translarna for the treatment of nmDMD and EMFLAZA for the treatment of Duchenne muscular dystrophy, statements with respect to 2019 net product revenue guidance and statements regarding: the future expectations, plans and prospects for PTC; expectations with respect to PTC's gene therapy platform, including any potential regulatory submissions; PTC's expectations with respect to the licensing and potential commercialization of Tegsedi and Waylivra; expansion of commercialization of Translarna and Emflaza; advancement of PTC's joint collaboration program in SMA, including any potential regulatory submissions; PTC's strategy, future operations, future financial position, future revenues, projected costs; and the objectives of management. Other forward-looking statements may be identified by the words "guidance", "plan," "anticipate," "believe," "estimate," "expect," "intend," "may," "target," "potential," "will," "would," "could," "should," "continue," and similar expressions.

PTC's actual results, performance or achievements could differ materially from those expressed or implied by forward-looking statements it makes as a result of a variety of risks and uncertainties, including those related to: the outcome of pricing, coverage and reimbursement negotiations with third party payors for Emflaza and Translarna and any other product candidates that PTC may commercialize in the future; whether, and to what extent, third party payors impose additional requirements before approving Emflaza prescription reimbursement; PTC's ability to complete any dystrophin study necessary in order to resolve the matters set forth in the denial to the Complete Response letter it received from the FDA in connection with its new drug application for Translarna for the treatment of nonsense mutation Duchenne muscular dystrophy (nmDMD), and PTC's ability to perform additional clinical trials, non-clinical studies, and CMC assessments or analyses at significant cost; PTC's ability to maintain its marketing authorization of Translarna for the treatment of nmDMD in the European Economic Area (EEA), including whether the European Medicines Agency (EMA) determines in future annual renewal cycles that the benefit-risk balance of Translarna authorization supports renewal of such authorization; PTC's ability to enroll, fund, complete and timely submit to the EMA the results of Study 041, a randomized, 18-month, placebo-controlled clinical trial of Translarna for the treatment of nmDMD followed by an 18-month open-label extension, which is a specific obligation to continued marketing authorization in the EEA; expectations with respect to the potential financial impact or PTC's ability to realize the anticipated benefits of the acquisition of Agilis and its gene therapy platform, including with respect to the business of Agilis and expectations with respect to the potential achievement of development, regulatory and sales milestones and contingent payments to the former Agilis equityholders with respect thereto and PTC's ability to obtain marketing approval of PTC-AADC and other product candidates acquired from Agilis, will not be realized or will not be realized within the expected time period; expectations with respect to the potential financial impact and benefits of the collaboration and licensing agreement with Akcea Therapeutics, Inc., including with respect to the timing of regulatory approval of Tegsedi and Waylivra in countries in LATAM and the Caribbean, the commercialization of Tegsedi and Waylivra, and PTC's expectations with respect to contingent payments to Akcea based on net sales and the potential achievement of regulatory milestones; the enrollment, conduct, and results of studies under the SMA collaboration and events during, or as a result of, the studies that could delay or prevent further development under the program, including any potential regulatory submissions with regards to Risdiplam; PTC's ability to realize the anticipated benefits of the acquisition of Emflaza, including the possibility that the expected benefits from the acquisition will not be realized or will not be realized within the expected time period; significant transaction costs, unknown liabilities, the risk of litigation and/or regulatory actions related to the acquisition of Emflaza or the acquisition of its gene therapy pipeline, as well as other business effects, including the effects of industry, market, economic, political or regulatory conditions; changes in tax and other laws, regulations, rates and policies; the eligible patient base and commercial potential of Translarna, Emflaza, PTC-AADC, Tegsedi, Waylivra, Risdiplam or any of PTC's other product candidates; PTC's scientific approach and general development progress; PTC's ability to satisfy its obligations under the terms of the senior secured term loan facility with MidCap Financial; the sufficiency of PTC's cash resources and its ability to obtain adequate financing in the future for its foreseeable and unforeseeable operating expenses and capital expenditures; and the factors discussed in the "Risk Factors" section of PTC's Annual Report on Form 10-K for the year ended December 31, 2017, Quarterly Reports on Form 10-Q for the periods ended March 31, 2018, June 30, 2018 and September 30, 2018 and Exhibit 99.2 to PTC's Current Report on Form 8-K filed on August 24, 2018, as well as any updates to these risk factors filed from time to time in PTC's other filings with the SEC. You are urged to carefully consider all such factors.

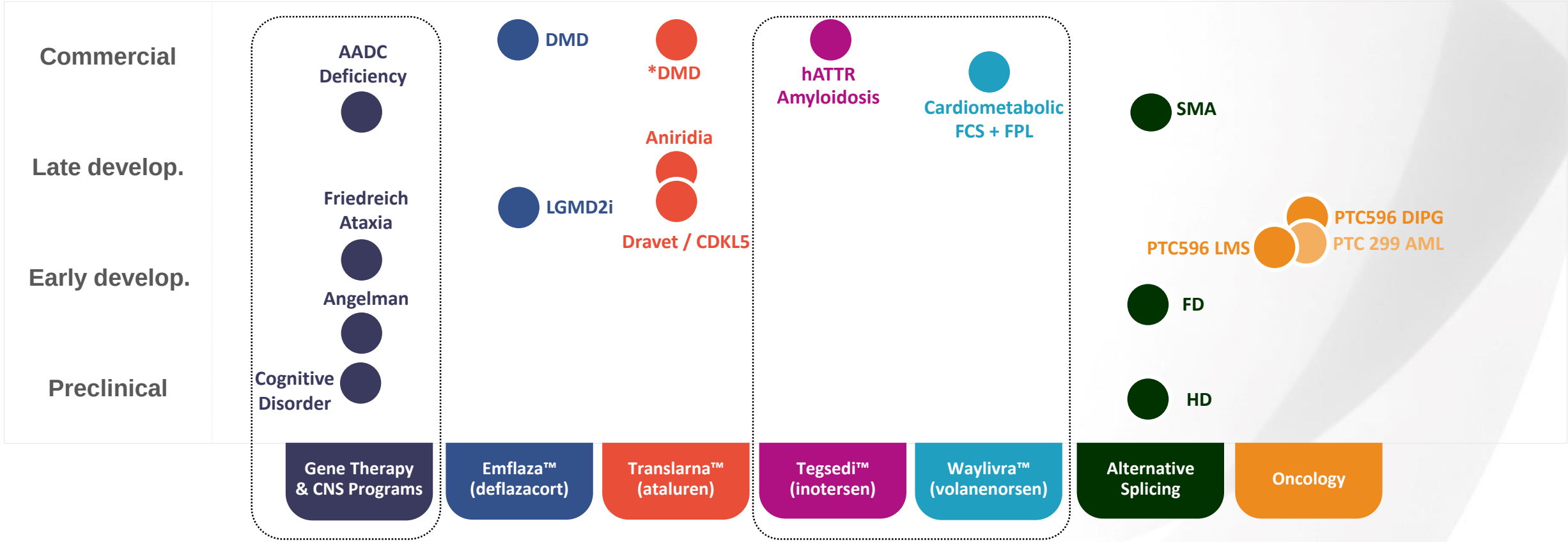
As with any pharmaceutical under development, there are significant risks in the development, regulatory approval and commercialization of new products. There are no guarantees that any product will receive or maintain regulatory approval in any territory, or prove to be commercially successful, including Translarna, Emflaza, PTC-AADC, Tegsedi, Waylivra or Risdiplam.

The forward-looking statements contained herein represent PTC's views only as of the date of this presentation and PTC does not undertake or plan to update or revise any such forward-looking statements to reflect actual results or changes in plans, prospects, assumptions, estimates or projections, or other circumstances occurring after the date of this presentation except as required by law.

# 2018: a transformational year



# Pipeline evolution: January 2019



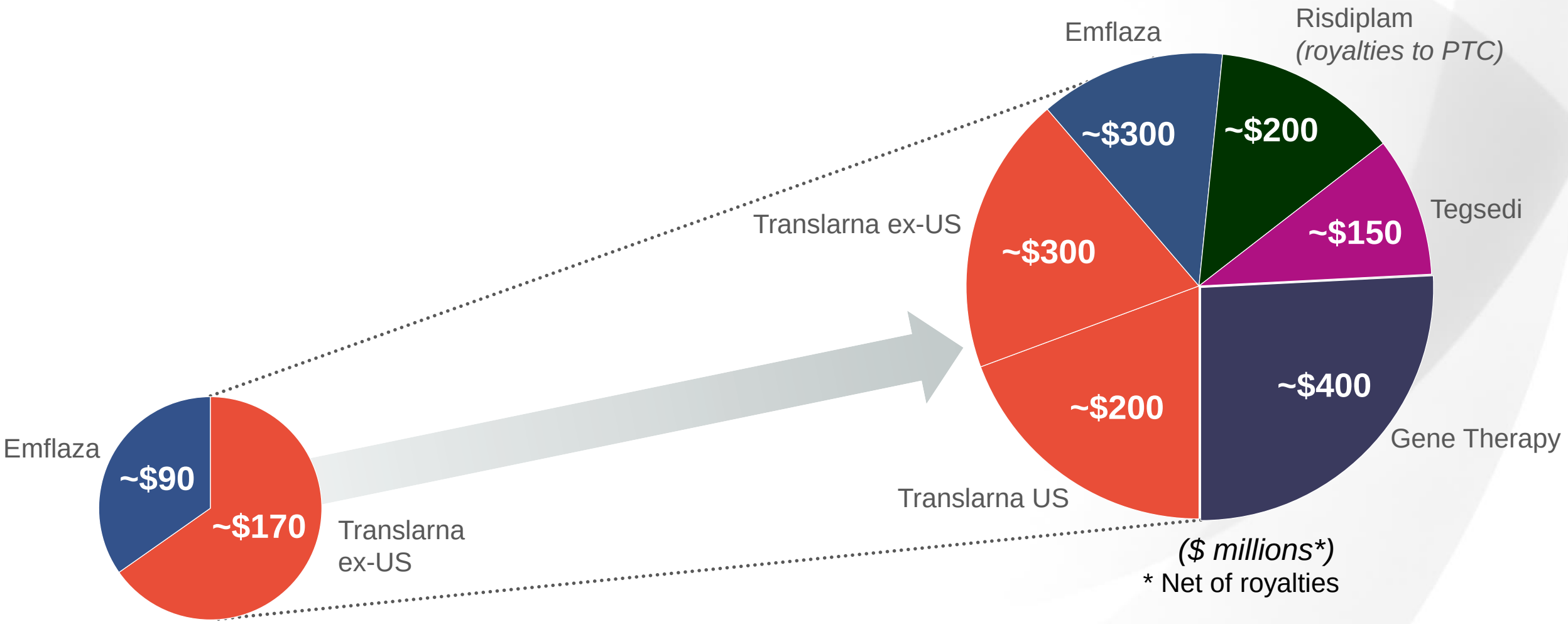

**Key 2018 Additions**

* MA requires annual renewal following reassessment by the European Medicines Agency (EMA)

# Looking forward:
# PTC growth vision for the next 5 years

| | *Now* | | *Future* |
|---|---|---|---|
| **COMMERCIAL**: | 2 products (Translarna and Emflaza) | **$263M** | **$~1.5B** (Translarna, Emflaza, Tegsedi, AADC, Risdiplam, FA) |
| **CLINICAL PROGRAMS:** | (AADC, SMA, Translarna, Emflaza, DIPG, AML) | **6** | **10** (AS, DIPG, AML, LMS, HD, FD, +4) |
| **RESEARCH PROGRAMS:** | (FA, AS, FD, HD, Reelin) | **5** | **20** (Small molecules, splicing, gene therapy and others) |
| **BD:** | Emflaza & Agilis acquisitions, Akcea in-licensing | **3** | ★ Opportunistic collaborations & BD in/out-licensing |

# ~$1.5B potential revenues to PTC by 2023






* Revenue based on PTC current assumptions and estimates

# Building a Leading Rare Disorder Biotech

## Global DMD Franchise

# PTC is the leader in DMD treatment
# 2 of 3 approved products

- Translarna is the first-ever targeted therapeutic approved for DMD anywhere in the world (EMA, 2014)
- Translarna is now available in >40 countries worldwide ex-US and in trials for US potential approval in 2020
- Emflaza is the first-and-only corticosteroid approved specifically for DMD anywhere in the world (US, 2017)
- Emflaza data demonstrates best-in-class corticosteroid
- PTC DMD franchise is now helping many thousands of families living with Duchenne around the world

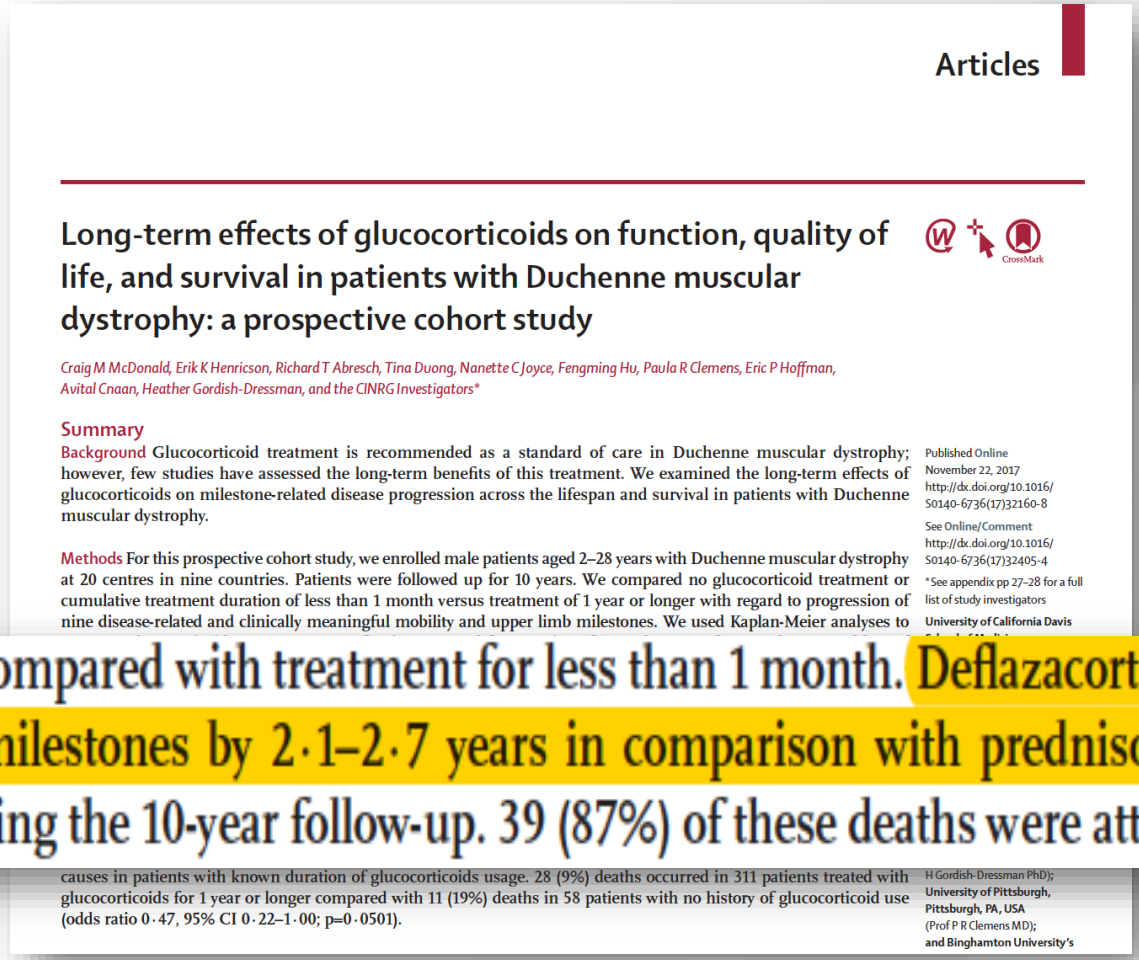
# Translarna™: proven track record of performance

- 2018 net product revenue of $171M, an 18% increase over 2017
- Global sales outside of the U.S.
- Pediatric expansion approved in 2018
- Label expansion for non-ambulatory patients under review
- U.S. dystrophin study underway, completion YE:19

# Emflaza®: Establishing standard of care for all DMD patients in the US

Emflaza® (deflazacort)

- 2018 Emflaza net product revenue of $91M
- Revenue increase of >$60M over 2017
- Data from multiple publications demonstrate Emflaza's clinical benefit over prednisone



Articles

Long-term effects of glucocorticoids on function, quality of life, and survival in patients with Duchenne muscular dystrophy: a prospective cohort study

Craig M McDonald, Erik K Henricson, Richard T Abresch, Tina Duong, Nanette C Joyce, Fengming Hu, Paula R Clemens, Eric P Hoffman, Avital Cnaan, Heather Gordish-Dressman, and the CINRG Investigators*

Summary

Background Glucocorticoid treatment is recommended as a standard of care in Duchenne muscular dystrophy; however, few studies have assessed the long-term benefits of this treatment. We examined the long-term effects of glucocorticoids on milestone-related disease progression across the lifespan and survival in patients with Duchenne muscular dystrophy.

Methods For this prospective cohort study, we enrolled male patients aged 2–28 years with Duchenne muscular dystrophy at 20 centres in nine countries. Patients were followed up for 10 years. We compared no glucocorticoid treatment or cumulative treatment duration of less than 1 month versus treatment of 1 year or longer with regard to progression of nine disease-related and clinically meaningful mobility and upper limb milestones. We used Kaplan-Meier analyses to

Published Online November 22, 2017 http://dx.doi.org/10.1016/S0140-6736(17)32160-8

See Online/Comment http://dx.doi.org/10.1016/S0140-6736(17)32405-4

*See appendix pp 27–28 for a full list of study investigators

University of California Davis

milestones by 2·8–8·0 years compared with treatment for less than 1 month. Deflazacort was as median age at loss of three milestones by 2·1–2·7 years in comparison with prednisone or p<0·012). 45 patients died during the 10-year follow-up. 39 (87%) of these deaths were attributal

causes in patients with known duration of glucocorticoids usage. 28 (9%) deaths occurred in 311 patients treated with glucocorticoids for 1 year or longer compared with 11 (19%) deaths in 58 patients with no history of glucocorticoid use (odds ratio 0·47, 95% CI 0·22–1·00; p=0·0501).

H Gordish-Dressman PhD); University of Pittsburgh, Pittsburgh, PA, USA (Prof P R Clemens MD); and Binghamton University's



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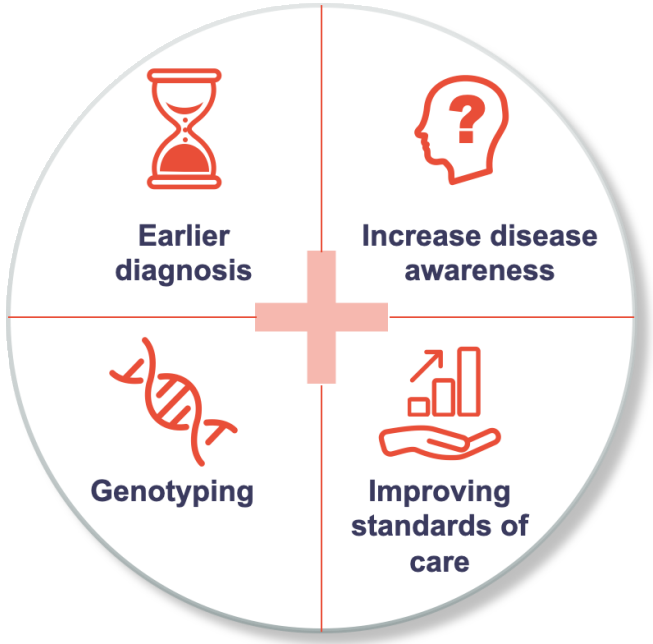
# Continuing to drive long-term growth of DMD franchise




translarna™
ataluren

**Label expansion under review for Translarna™ in non-ambulatory patients by the EMA**

**sNDA for Emflaza® 2-5 year old U.S. patients submitted with potential approval in ‘19**

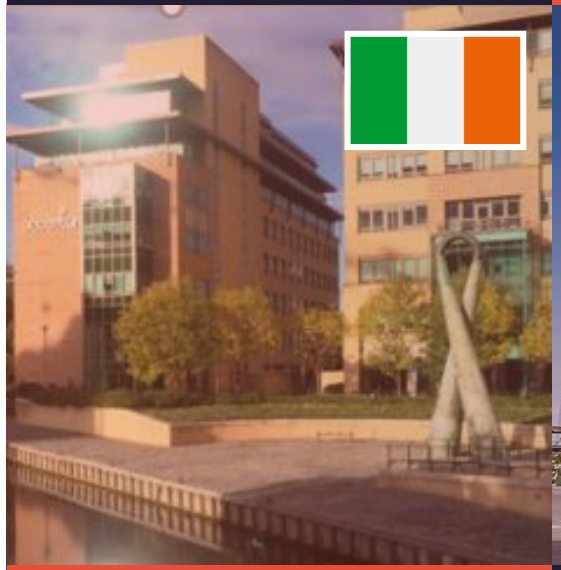
Emflaza™
(deflazacort)

# An efficient, scalable business engine

- 2018 net product net revenue of $263M
- 2019 DMD franchise revenue guidance of $285 - $305M
- Established footprint in >40 countries worldwide
- Experienced commercial and medical teams in orphan disease
- Fully integrated global infrastructure


South Plainfield, New Jersey


Zug Switzerland, Marketing, Medical and Regulatory Hub



Dublin, Ireland International HQ


Latam Regional Office, Sao Paulo, Brazil

# Building a Leading Rare Disorder Biotech

## Leveraging our Global Commercial Franchise

# Preparing for successful launch

Tegsedi™ (inotersen) injection 284 mg/1.5 mL

**Tegsedi best fit for Latin American hATTR market**

hATTR polyneuropathy most prevalent phenotype in Latin America
~6,000 patients

Sub-cutaneous self administration preferable to infusions in the region

**Diversifies our rare disease portfolio and revenues**

**All key hiring completed in Latam**

**Regulatory dossier filed with ANVISA and rare-disease priority review granted**

**Expected approval YE:19**

PTC THERAPEUTICS

# Two potential assets in Latin America

Tegsedi™ (inotersen) injection 284 mg/1.5 mL

**Tegsedi best fit for Latin American hATTR market**

hATTR polyneuropathy most prevalent phenotype in Latin America
~6,000 patients

Sub-cutaneous self administration preferable to infusions in the region

**Diversifies our rare disease portfolio and revenues**

waylivra™ (volanesorsen sodium) Injection 300mg in 1.5mL

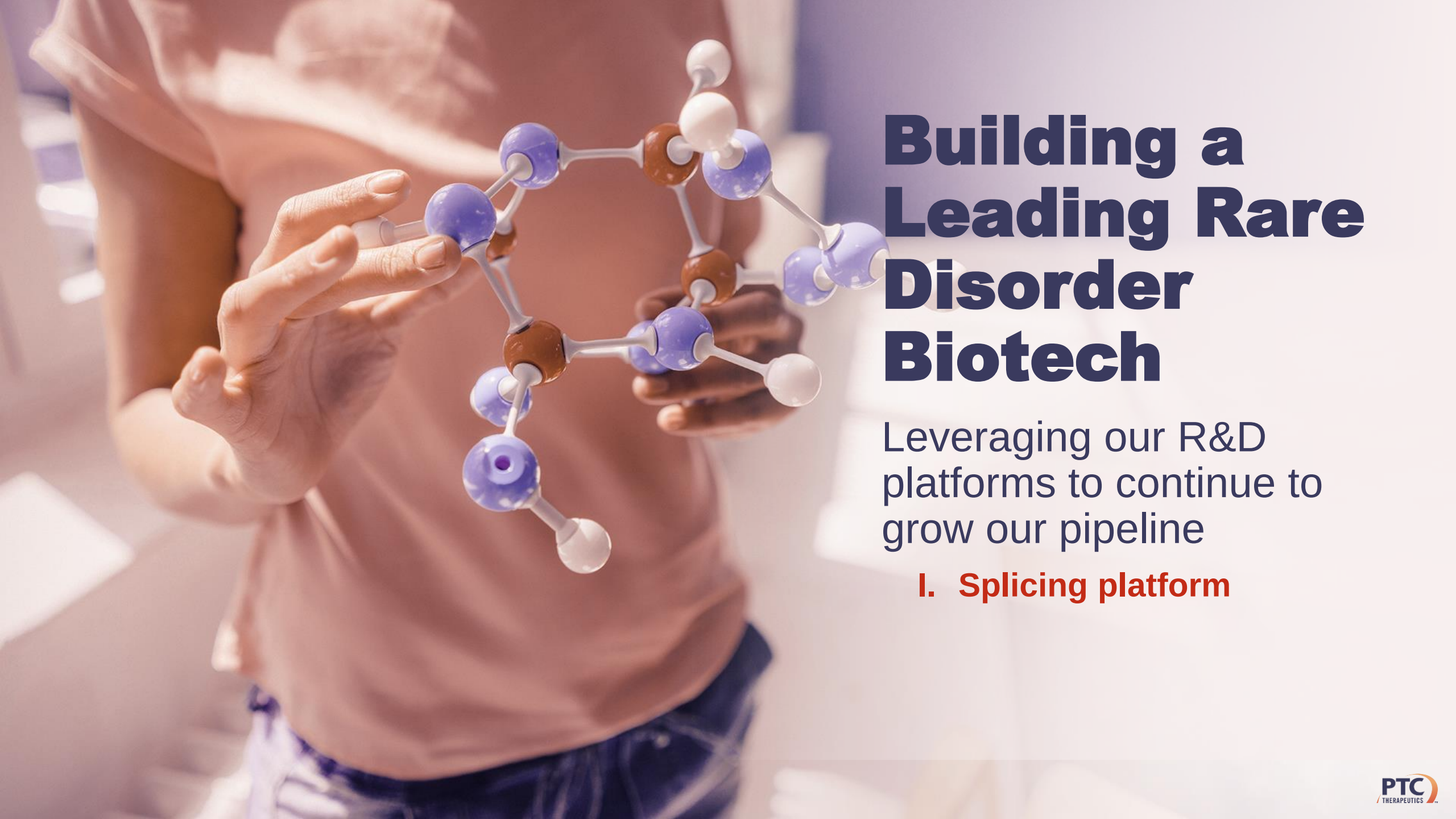
**Waylivra: could utilize our patient support in Latin America**

Similar economic opportunity to Translarna in Latin America

No other treatments available to treat FCS

Received positive CHMP opinion

FCS = familial chylomicronemia-syndrome
FPL = familial partial lipodystrophy



# Building a Leading Rare Disorder Biotech

Leveraging our R&D platforms to continue to grow our pipeline

I. **Splicing platform**

# Leaders in small molecule RNA-splicing technology

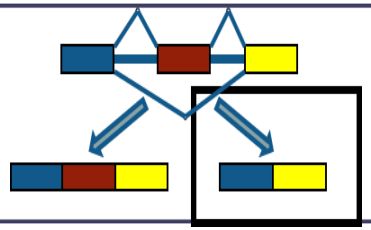
Development of SMA candidate as potential best-in-class treatment

13 years of discovering and developing drugs that target pre-mRNA splicing

Cutting-edge tech platform discovered and developed by PTC

**2nd Splicing Compound: A Development Candidate to treat Familial Dysautonomia**

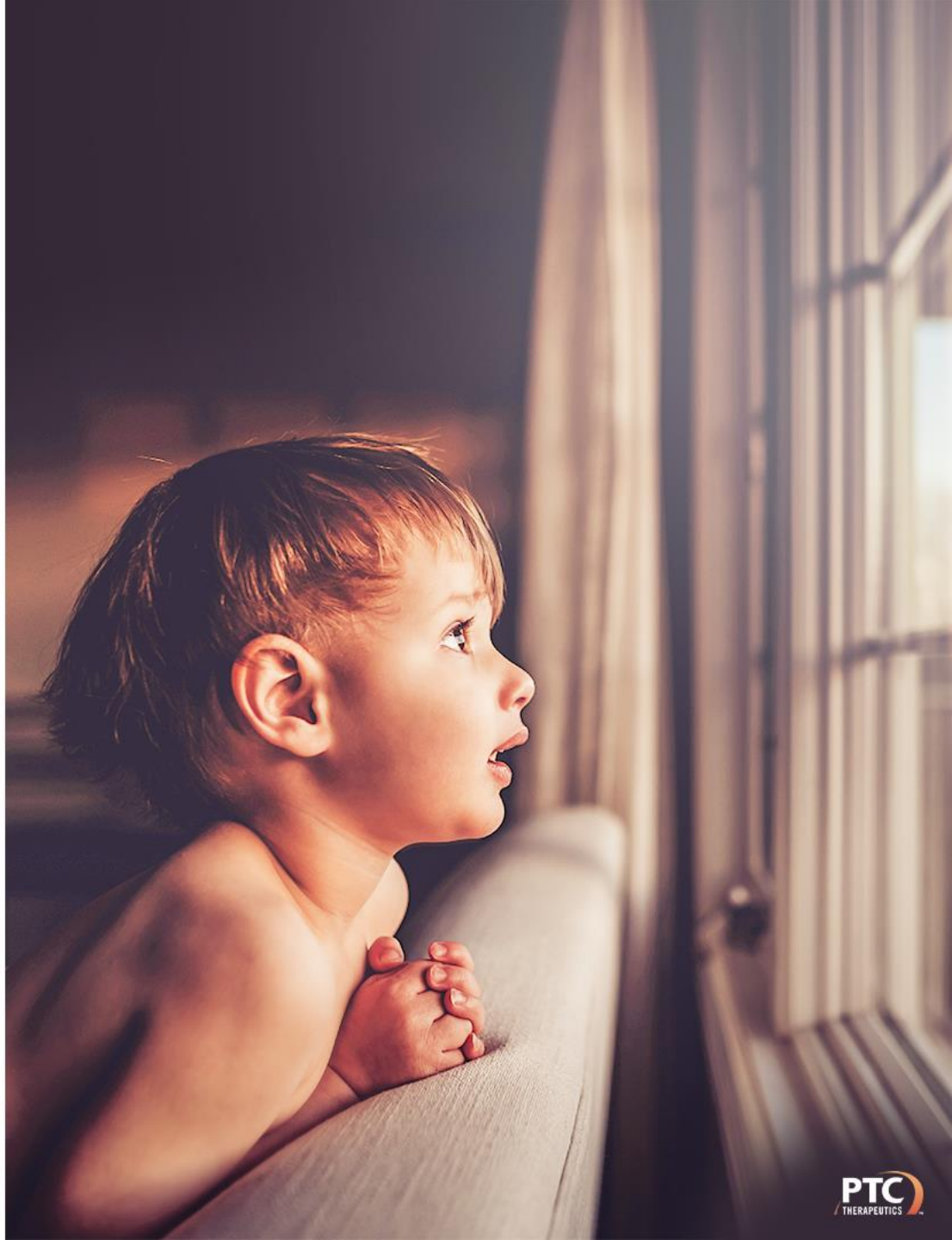
Continue to exploit Splicing platform; addressing additional areas of unmet need

| Platform | Mechanism Targeted | Programs |
|---|---|---|
| Splicing |  Target-splicing events to restore or decrease protein levels | **SMA – SMN2**<br>**FD – IKBKAP**<br>**HD – HTT**<br>**Others** |

# Risdiplam in development for Spinal Muscular Atrophy (SMA)

- Primary genetic cause of infant mortality
- Small molecule promotes the correct splicing of the mutant RNA
- Small molecule has potential for best in class therapy
- Broad tissue distribution and protein restoration

**Risdiplam targets-splicing events to restore SMN protein levels**



# Risdiplam has potential to be > $2B product

- Revenue > $1B subject to mid-teens* royalty to PTC from Roche
- Potential to PTC to exceed $200M/ year; including competitive assumptions for SMA gene therapy
- Firefish & Sunfish fully enrolled
- Risdiplam well tolerated at all doses, no ocular toxicity found in humans

*** Revenue estimates based on PTC solely on assumptions**
Full tiered royalty table in press release

**Based on FDA feedback:**

**Data from Sunfish & Firefish part 1 should be sufficient for NDA filing**

**Plan to file in 2019**

# The splicing technology is a proven platform to identify new therapeutics

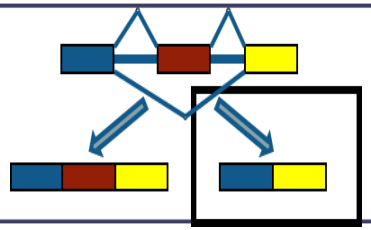
Development of SMA candidate as potential best-in-class treatment

13 years of discovering and developing drugs that target pre-mRNA splicing

Cutting-edge tech platform discovered and developed by PTC

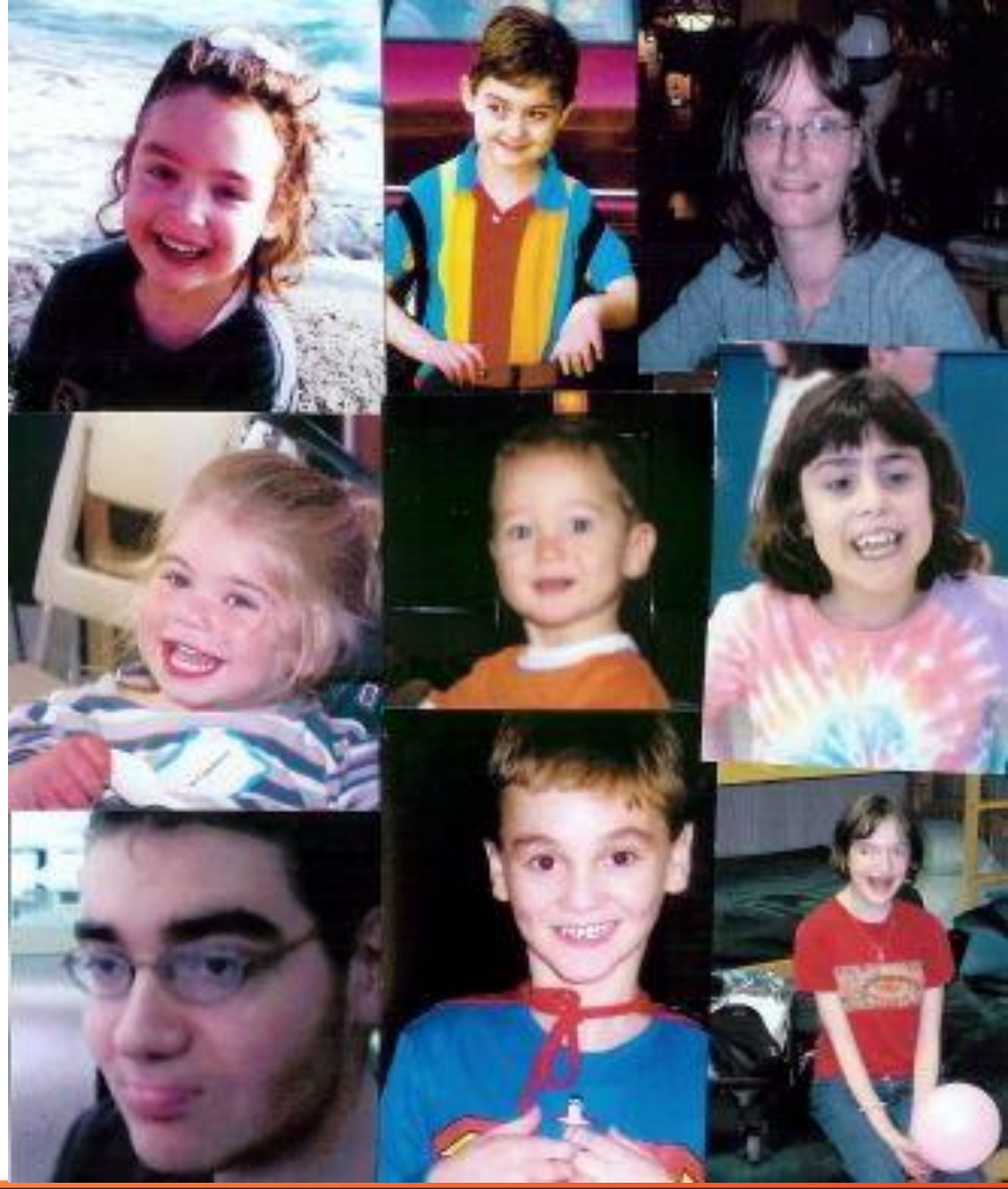
**2nd splicing compound: A development candidate to treat Familial Dysautonomia**

**Continue to exploit splicing platform; addressing additional areas of unmet need**

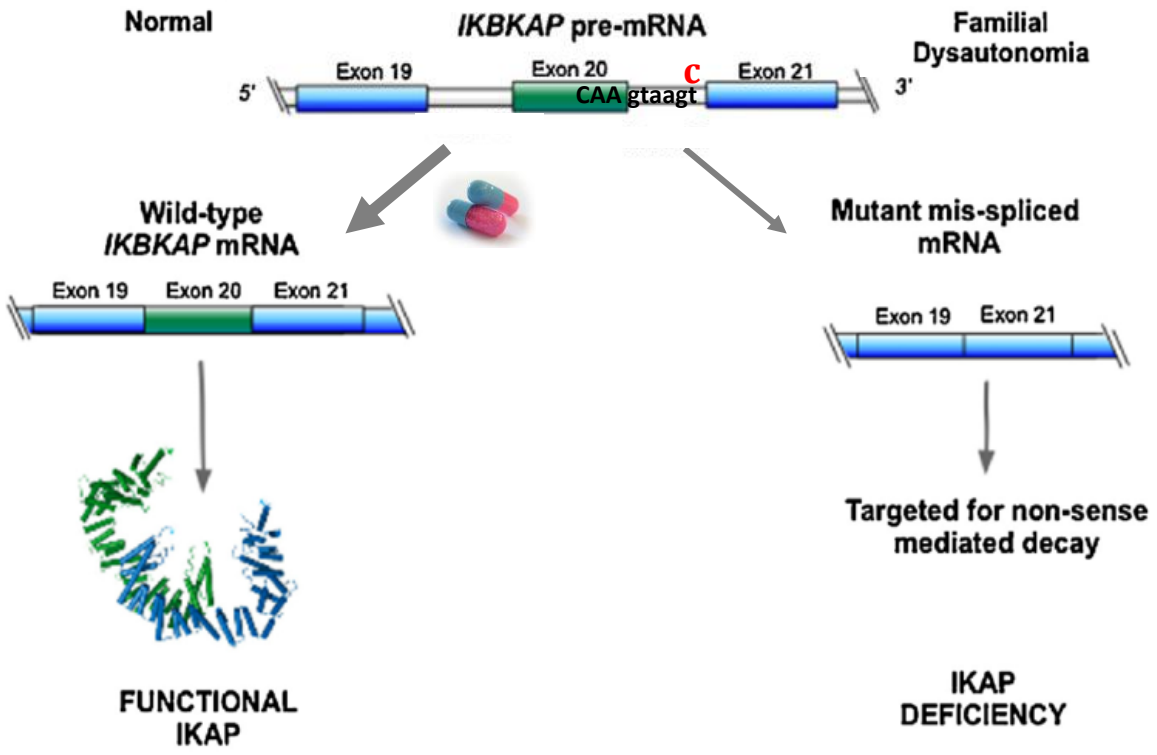
| Platform | Mechanism Targeted | Programs |
| --- | --- | --- |
| Splicing |  Target-splicing events to restore or decrease protein levels | SMA – SMN2<br>FD – IKBKAP<br>HD – HTT<br>Others |

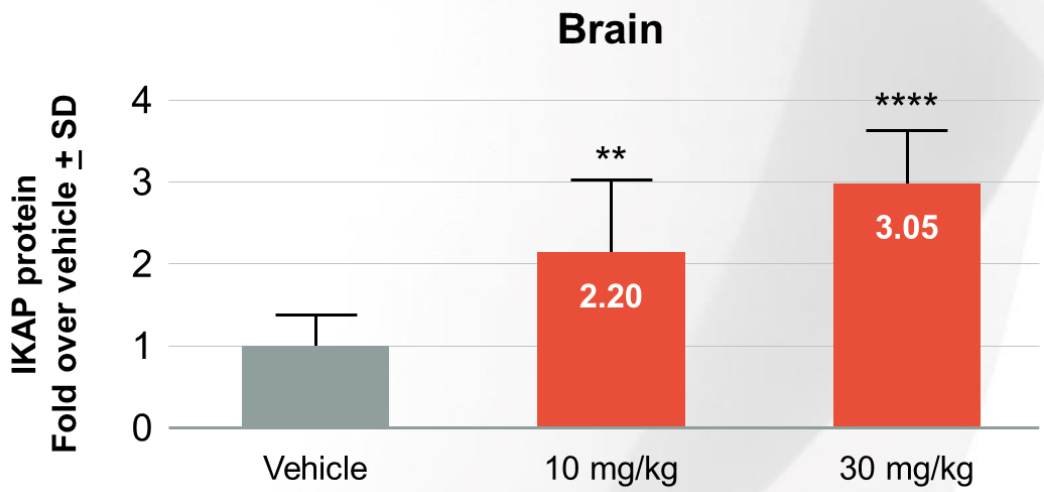
# Familial dysautonomia:

- Genetic disorder primarily affecting the sensory and autonomic neurons
- Caused by a splicing-altering mutation in the IKBKAP (ELP1) gene resulting in low levels of IKAP protein
- Ashkenazi Jewish ancestry, carrier frequency is ~1:30
- No therapies are currently available for FD, only supportive treatments
- PTC is collaborating with MGH and NYU to advance treatments for FD

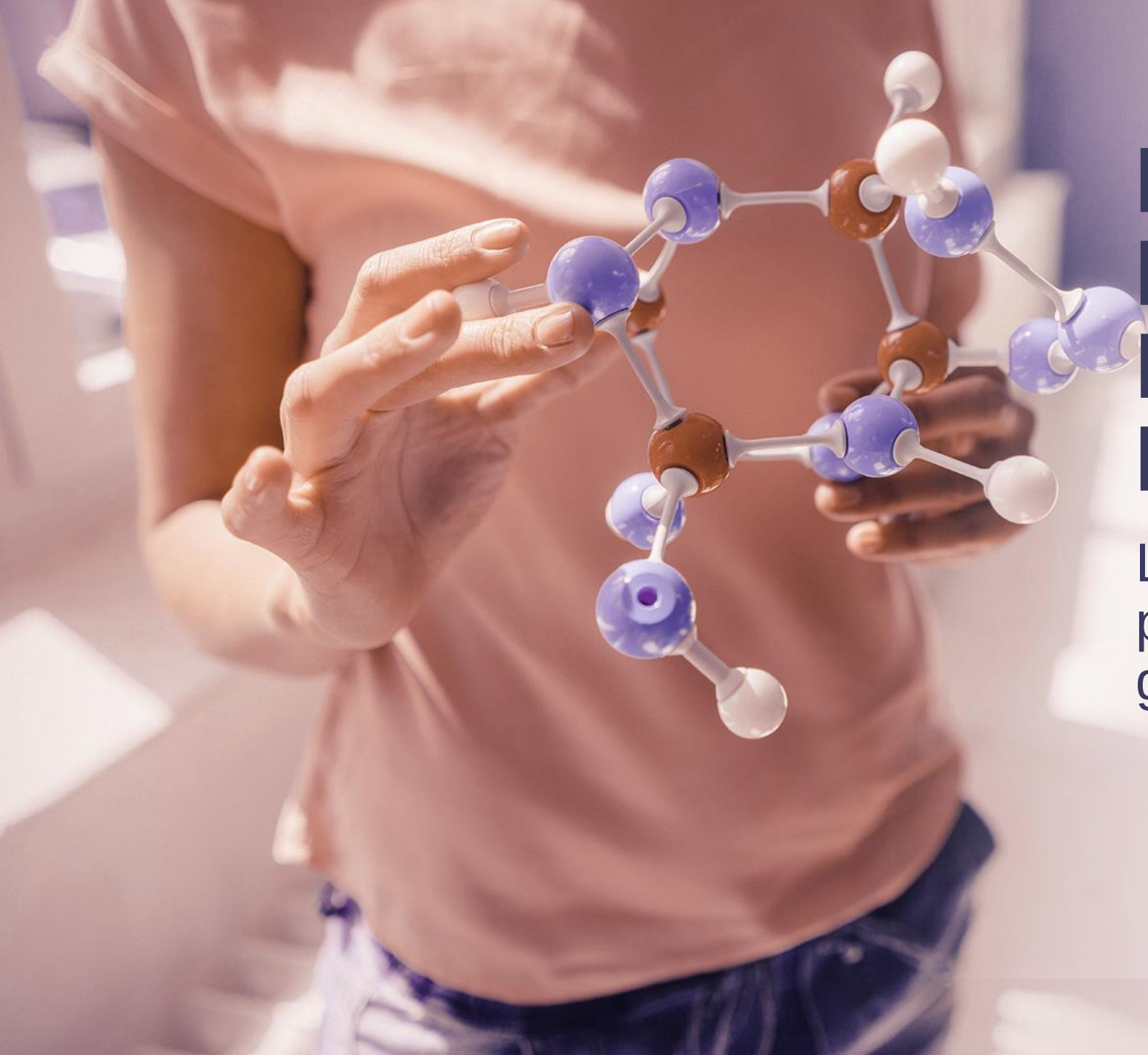


# PTC-258 splicing modifiers restore IKAP levels




**Development candidate PTC-258 selected YE:18**
**Scheduled to enter the clinic in 2019**



# Building a Leading Rare Disorder Biotech

Leveraging our R&D platforms to continue to grow our pipeline

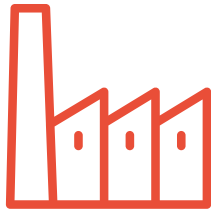
II. **A CNS gene therapy platform**

# Gene therapy development strategy

Execute on current programs

Target dates:

- *AADC Launch 2020*
- *Friedreich Launch 2023*
- *Angelman IND 2020*
- *Reelin IND 2020*



Priority to secure in-house manufacturing capabilities to support long-term capacity

Expand the pipeline with internal research and external collaboration

# AADC deficiency is a devastating disease with high unmet need

- Rare progressive childhood disease, affecting approximately 5,000 patients globally
- Children with attenuated AADC deficiency never achieve motor development milestones
- Profound development failure with shortened life expectancy in attenuated forms (4 - 8yrs)

| | Head Position 3-4 months | Sitting 6-9 months | Standing 10-12 months |
|---|---|---|---|
| Normal | ✓ | ✓ | ✓ |
| Attenuated AADC | ⊘ | ⊘ | ⊘ |

Wassenberg T et al. *Orphanet J Rare Dis*. 2017;12(1):12

# AADC deficiency patient
# Before and after treatment with PTC-AADC

*Case 5  T0 (2 yo)*

*In part:  Science Translational Medicine 16 May 2012 Vol 4 Issue 134 134ra61*

# AADC deficiency patient
# Before and after treatment with PTC-AADC

*Case 5 T0 (2 yo)*

*T13 (3 yo)*

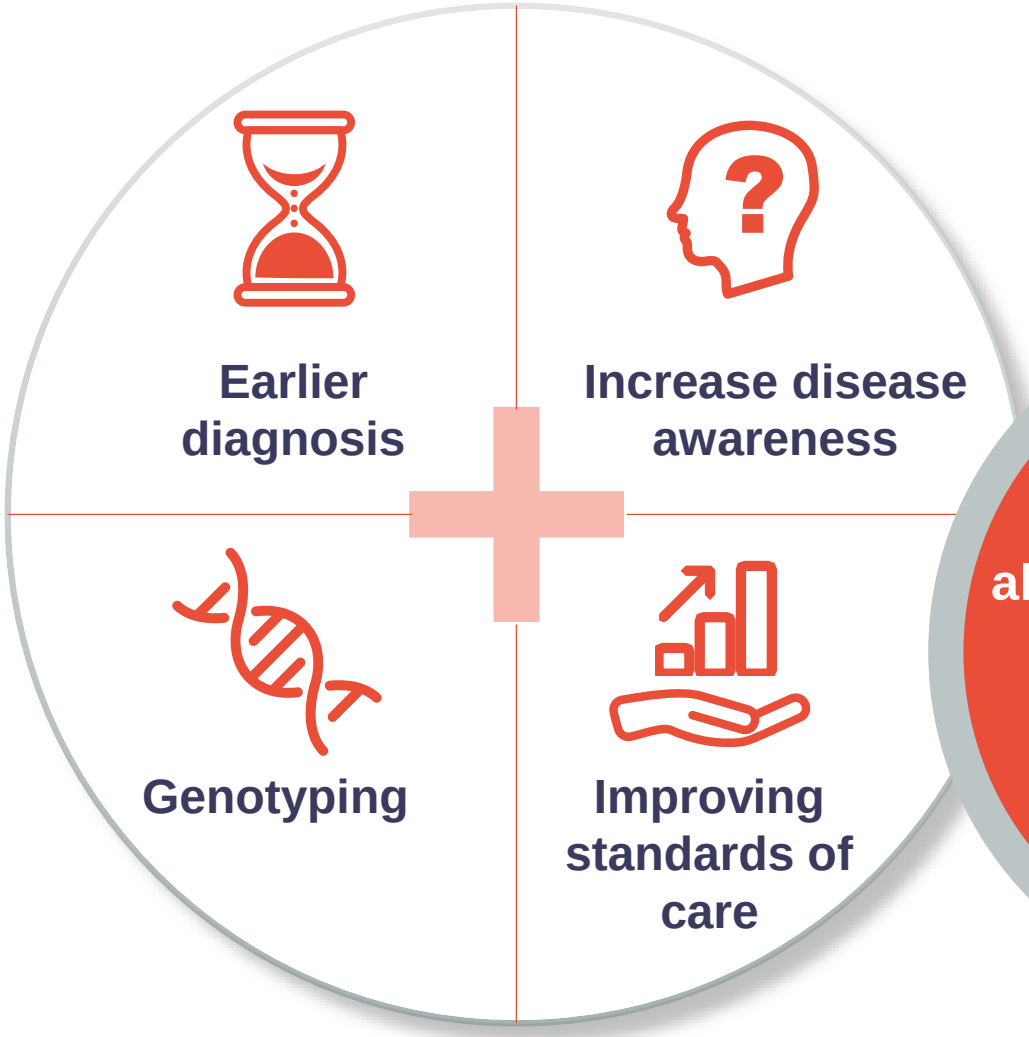
*In part: Science Translational Medicine 16 May 2012 Vol 4 Issue 134 134ra61*

# AADC deficiency patient
# Before and after treatment with PTC-AADC

*Case 5 T0 (2 yo)* *T13 (3 yo)* *T29 (4 yo)*

*In part: Science Translational Medicine 16 May 2012 Vol 4 Issue 134 134ra61*

# Patient identification is our expertise




**~100**

**AADC patients already identified in the US and Europe**

- Genotyping patients in seizure and cerebral palsy clinics
- Plan to screen >100K at-risk patients for AADC

# Most advanced FA gene therapy program

## PTC plans to file IND in 2019

Targeted Micro dosing / direct to CNS

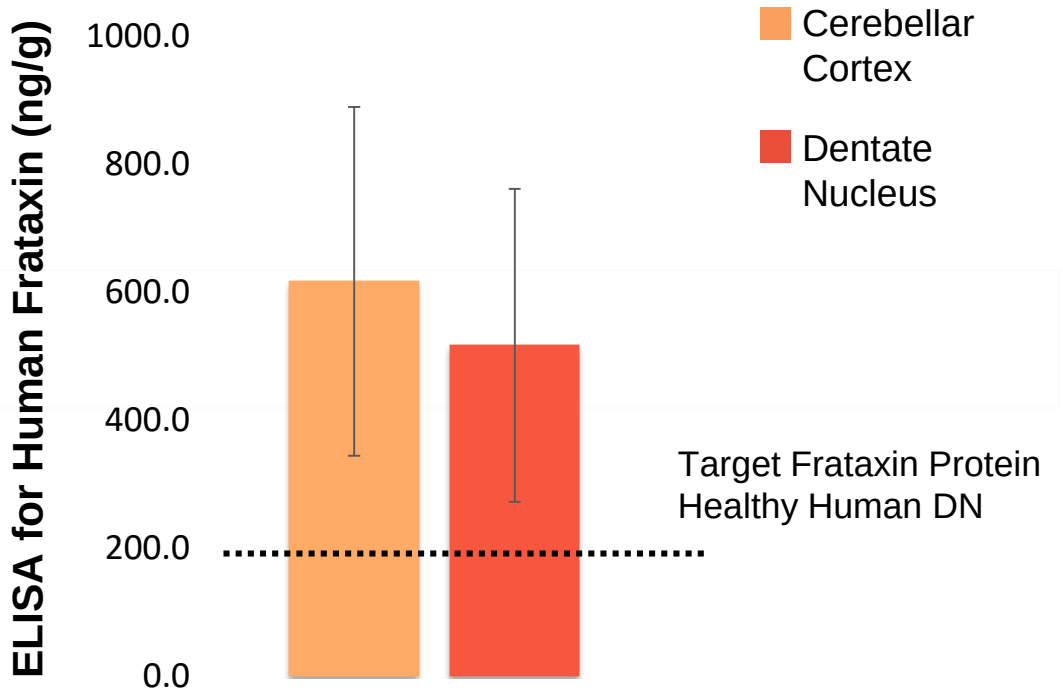
Favorable immunogenic profile

Animal data supports appropriate dose

Patient group engagement

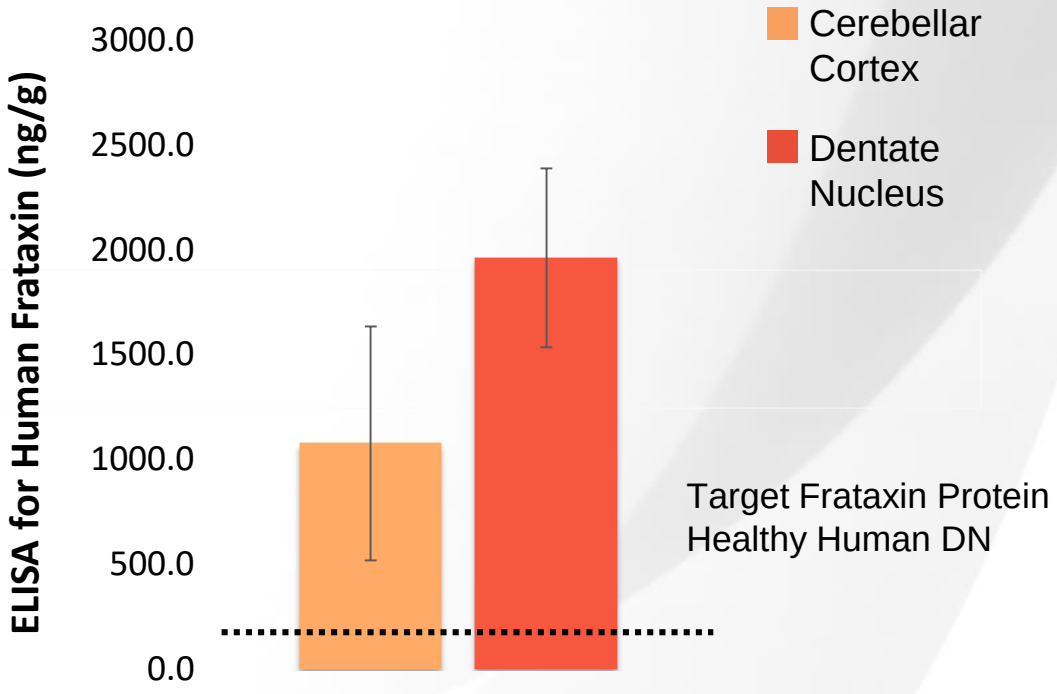
# Moving toward IND filing in 2019

## PTC-FA Intracerebellar Dosing in Porcine Model*




Unilateral dose of 3.0 x $10^{12}$ vg total - Day 28 Mean (SEM)
*Human-specific detection

## PTC-FA Intracerebellar Dosing in NHP Model*

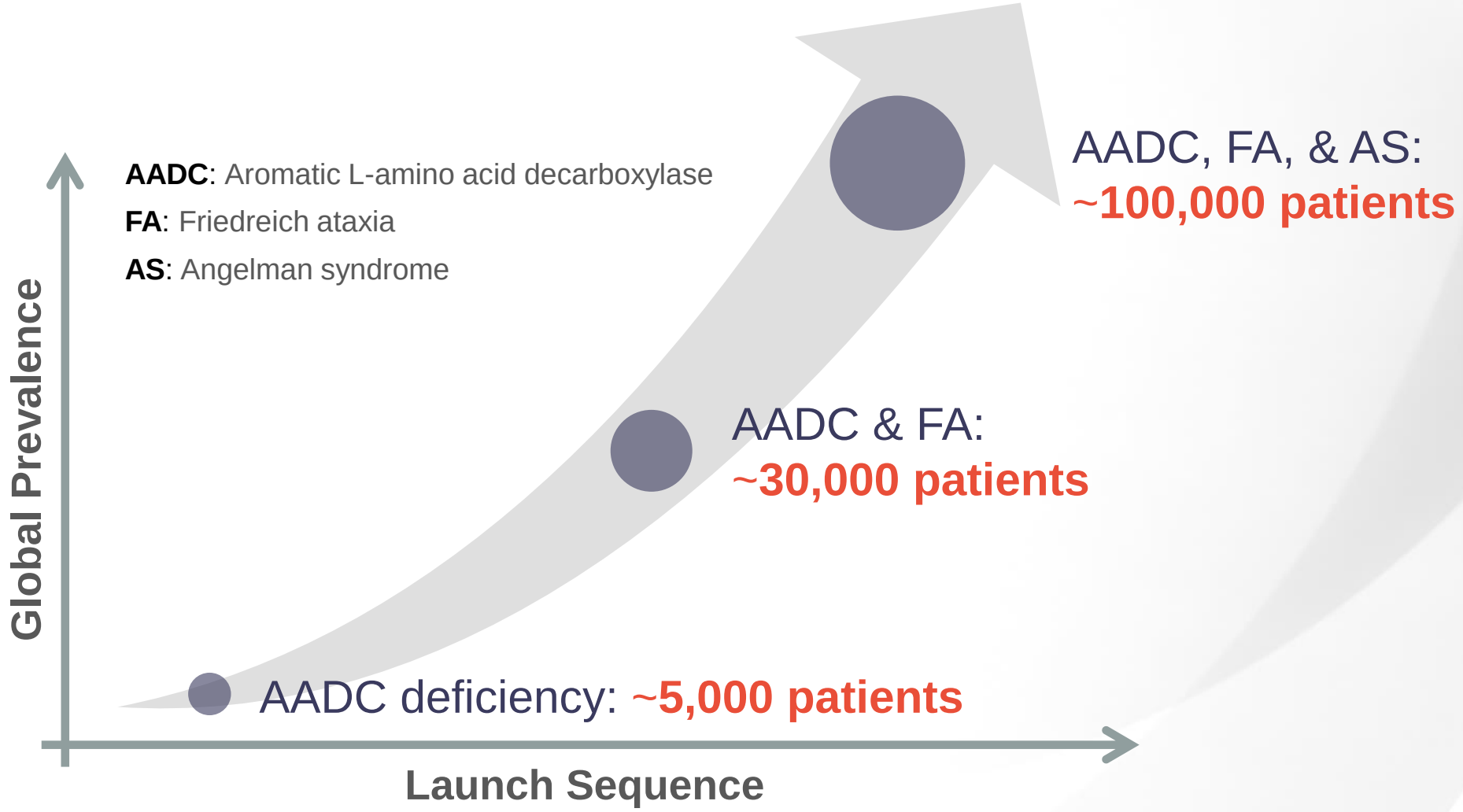



Bi-lateral Dose of 2.4 x $10^{12}$ vg total - Day 28 - Mean (SEM)
*NHP background subtracted

# 2019 goals: submit an AADC BLA & FA IND


**Immediate clinical manufacturing capabilities** as well as the **plan to expand** to commercial scale

# Potential addressable market in excess of $5B

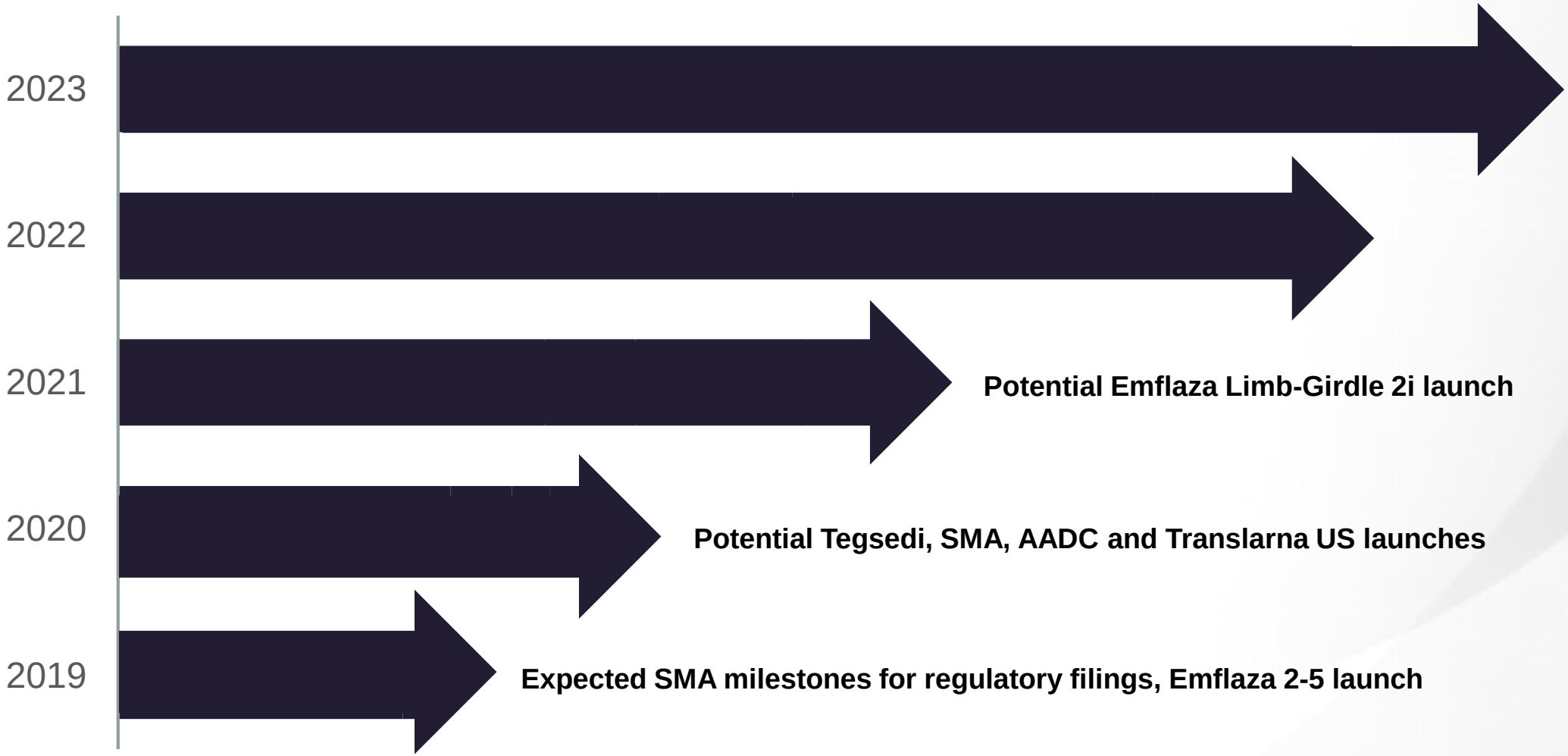


# Niche oncology strategy prioritizes value creation

| | |
|---|---|
| **Internal research** | Use of current platforms to add new targets to portfolio with focus on splicing |
| **Solid tumors** | PTC596 in pediatric brain tumor (DIPG) phase 1/2 trial and Leiomyosarcoma (LMS) |
| **Hematologic malignancies** | PTC299 AML dose escalation trial initiated in 2018 |
| **Business development** | Assess out-licensing opportunities |

# Sustainable growth expected over next 5 years

## Potential revenues to PTC from DMD franchise, Gene therapy programs, Tegsedi and Risdiplam



# *measured by moments*

Everyone has a different definition of progress. For the last 20 years, we've measured our progress researching rare disease in moments. Smiling ones and crying ones. Moments spent with our boys' families and ones with their friends. We know that every step forward comes after several steps backward, because we've lived it—whether spending time with families in their homes or with our scientists researching in our labs.

It can be easy to lose yourself as you progress further. Although we've grown, our heart remains in the same place, because we've never measured ourselves like larger companies do. Our biggest accomplishment has always been the time we can give to all of our families. Whether it's hours, days, months, or years, every small moment is a big win.

PTC THERAPEUTICS