PTC Therapeutics: 20 years of commitment to bringing new treatments to patients with rare disorders

JANUARY 2018

Forward looking statements within the meaning of The Private Securities Litigation Reform Act of 1995

All statements, other than those of historical fact, contained in this presentation, are forward-looking statements, including statements regarding: the future expectations, plans and prospects for PTC; PTC's preliminary 2017 unaudited results; PTC's financial guidance for 2018; PTC's plans for further interactions with the FDA regarding the Translarna NDA; the outcome of any formal dispute resolution request filed with the FDA; the size of the DMD patient population eligible for Emflaza treatment in the U.S.; expansion of Translarna globally; the timing of, and PTC's ability to, expand the approved product label of Translarna for the treatment of nmDMD in the EEA, in pediatric patients, or otherwise; advancement of PTC's studies of Translarna for the treatment of other indications and its other pipeline programs; advancement of PTC's joint collaboration program in SMA; the clinical utility and potential advantages of Translarna (ataluren) and Emflaza™ (deflazacort); PTC's strategy, future operations, future financial position, future revenues or projected costs; and the objectives of management. Other forward-looking statements may be identified by the words "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: 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, 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 outcome of pricing, coverage and reimbursement negotiations with third party payors for Emflaza and Translarna; whether, and to what extent, third party payors impose additional requirements before approving Emflaza prescription reimbursement; PTC's ability to resolve the matters set forth in the Complete Response letter it received from the FDA in connection with its NDA for Translarna for the treatment of nmDMD either via outcome of any formal dispute resolution request or other interactions with the FDA, 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; the eligible patient base and commercial potential of Translarna, Emflaza and PTC's other product candidates; the enrollment and conduct 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; 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 most recent Quarterly Report on Form 10-Q 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 or Emflaza.

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.

Our vision

Our mission

To bring best in-class therapies with **clinical benefit** to **patients** affected by **rare disorders**

Our strategy

To leverage our global commercial infrastructure to **maximize value for patients and all stakeholders**

Sustainable, growing DMD business enables continued innovation & growth

Total 2017 unaudited revenue of $195 million

1) Growing global DMD franchise with unaudited 2017 revenue of $174 million

- Translarna™ strong continued patient uptake reflected in annual growth
- Emflaza™ impressive launch; opportunity to establish standard of care

($ million)	2017 Unaudited Revenue	2018 Financial Guidance
Translarna	$145	$170 - $185
Emflaza	$29	$90 - $110
DMD Franchise	**$174**	**$260 - $295**

2) Leveraging internal splicing technology platform

- Spinal Muscular Atrophy program in pivotal stage; triggered $20 million milestone in Q4:17
- Huntington's Disease program developing

Survival data on SMA Type 1 babies will be presented at EU SMA congress in January 2018

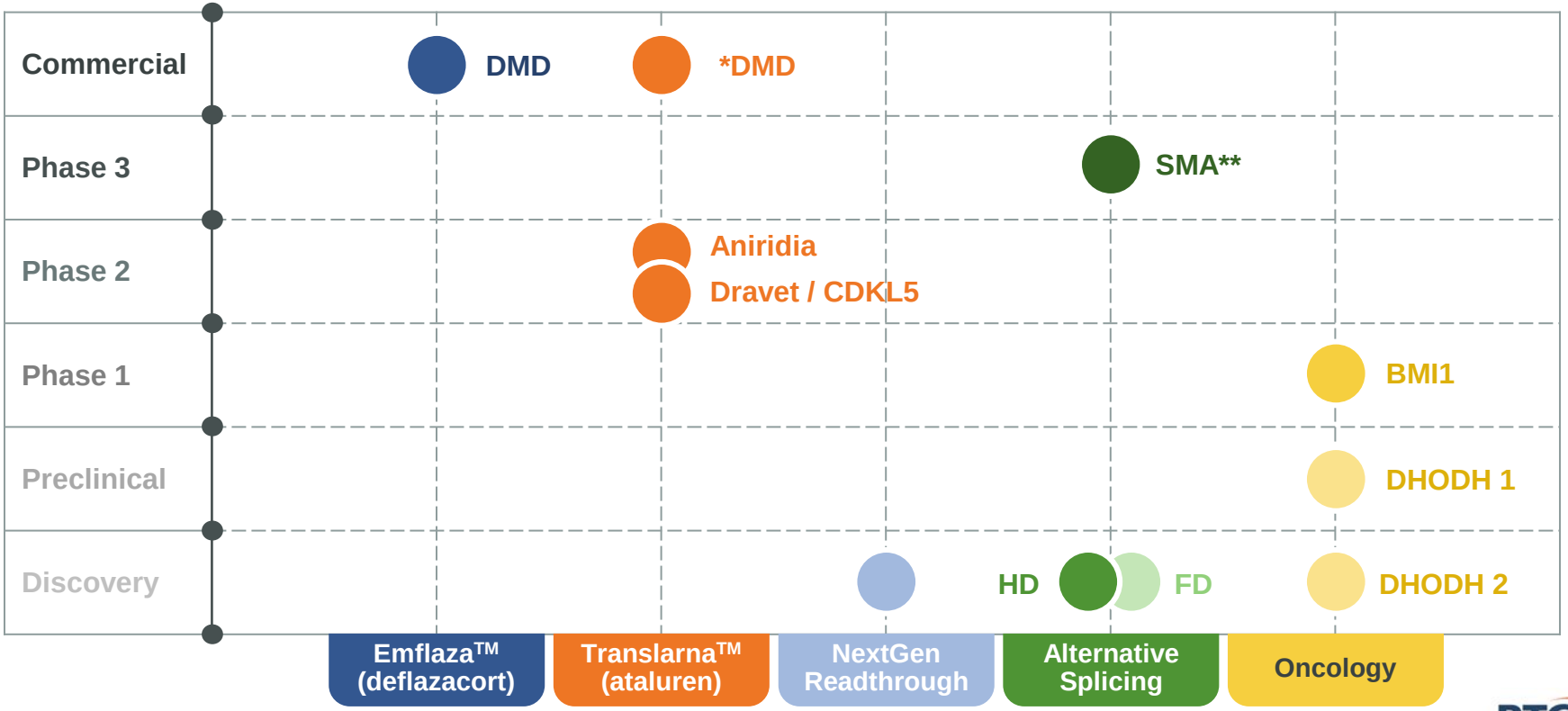
3) Pursuing internal and in-licensing value-creation opportunities

- Leverage our strong global commercial infrastructure

Poised to pursue new assets and maximize value

PTC THERAPEUTICS™ 20 YEARS OF COMMITMENT

Expanding pipeline through in-house innovation



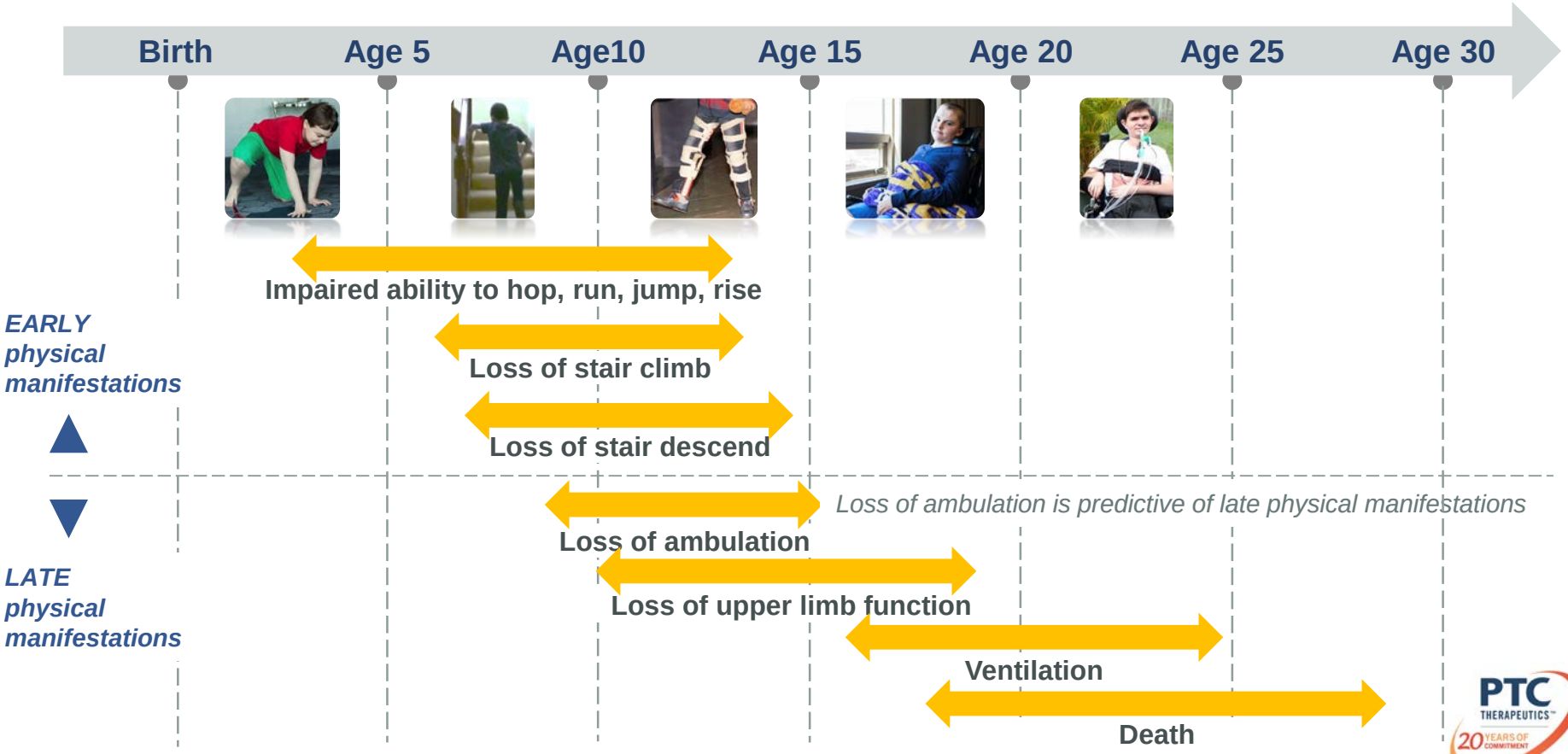
* MA requires annual renewal following reassessment by the European Medicines Agency (EMA)

** Phase 3 Sunfish clinical study of RG7916 in SMA type 2/3 patients began in Nov 2016, Firefish pivotal stage in SMA type 1 patients to begin in coming months

Translarna™ & Emflaza™

Transforming the standard of care for DMD patients

DMD progression is sequential, non-linear and irreversible



Translarna™: Addressing the underlying cause of nonsense mutation Duchenne Muscular Dystrophy

Birth | Age 2 | Age 5+ | .....

translarna™ ataluren

1:4,000 males DMD

~10-15% nonsense mutation

Disease awareness, genetic testing and early treatment are critical

Translarna delays time to loss of ambulation & pulmonary function

Delay to ventilation correlated to delay of loss of life

Efforts underway for label expansion

>7,000* patients under current label** outside the U.S.

Patients are diagnosed worldwide far too late
Label expansion efforts underway for earlier treatment

PTC THERAPEUTICS™ 20 YEARS OF COMMITMENT

Establishing Emflaza™ : Establishing as part of standard of care for U.S patients

Emflaza™ (deflazacort)

Birth | Age 2 | Age 5+ | .....

1:4,000 males DMD

Initiating treatment at diagnosis

Emflaza delays loss of ambulation by 4 years

Continued use beyond loss of ambulation preserves pulmonary function

Emflaza is a critical component of DMD treatment

Efforts underway for label expansion to 2 years of age

First approved in the U.S. for use in all DMD patients
5 years+ regardless of genetic mutation
9,000 U.S. DMD eligible patients

Earlier / longer treatment extends time to loss of function

PTC THERAPEUTICS™ 20 YEARS OF COMMITMENT

Translarna™: Proven track record of successful global sales

- Unaudited 2017 net revenue of $145 M
- Guidance for 2018 of $170 - $185 M
- Global sales outside of the U.S. since 2014
- Pediatric expansion under EMA review
- U.S. appeal process underway, expect update in Q1

~15%

Expected 5 year (12/31/17-12/31/22) CAGR

PTC THERAPEUTICS™ 20 YEARS OF COMMITMENT

Emflaza™: Establishing standard of care for all DMD patients in the U.S.

Emflaza™
(deflazacort)

- 2017 Emflaza unaudited net sales of $29 M
- Guidance for 2018 of $90 - $110 M
- Results from Lancet publication reinforce Emflaza efficacy differentiation

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 compare glucocorticoid treatment groups for time to stand from supine of 5 s or longer and 10 s or longer, and loss of stand from supine, four-stair climb, ambulation, full overhead reach, hand-to-mouth function, and hand function. Risk of death was also assessed. This study is registered with ClinicalTrials.gov, number NCT00468832.

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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 School of Medicine, Sacramento, CA, USA
(Prof C M McDonald MD, E K Henricson PhD, R T Abresch

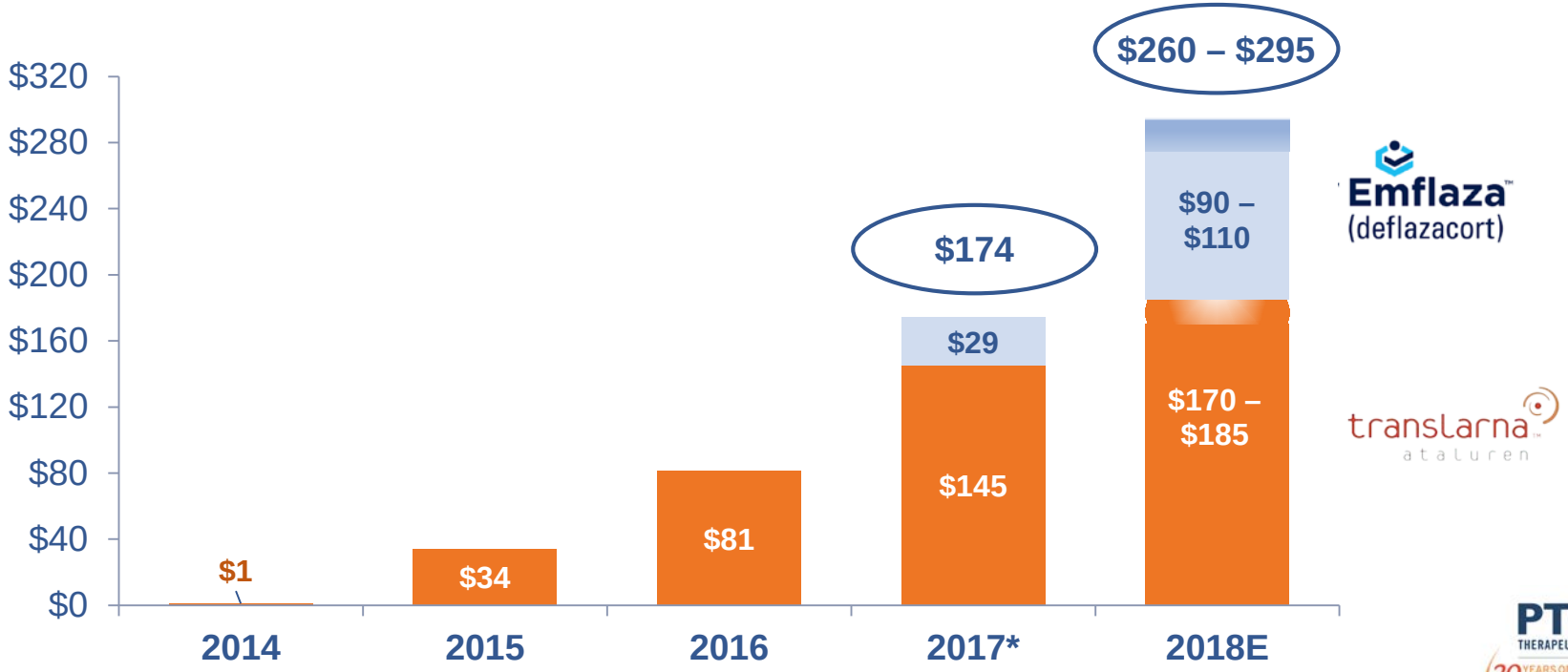
milestones by 2·8–8·0 years compared with treatment for less than 1 month. Deflazacort was associated with increased median age at loss of three milestones by 2·1–2·7 years in comparison with prednisone or prednisolone (log-rank p<0·012). 45 patients died during the 10-year follow-up. 39 (87%) of these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

PTC THERAPEUTICS™ 20 YEARS OF COMMITMENT

Growing global DMD franchise

Translarna™ & Emflaza™ DMD Net Sales

($ in millions)



- Unaudited

Improving patient outcome by delivering best in class therapy earlier to preserve function

Earlier diagnosis

Increase disease awareness

Genotyping

Improving standards of care

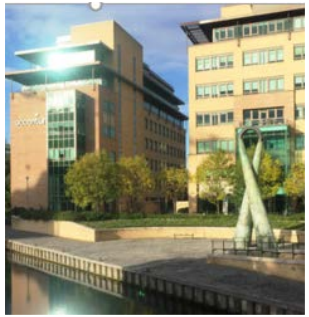
Pursuing label expansions to bring Emflaza™ & Translarna™ to younger patients to ultimately improve patient outcome

An efficient, scalable commercialization engine

- 2017 unaudited product net sales of $174 M
- Established footprint in 47 countries worldwide
- Experienced commercial team in orphan disease
- Fully integrated global commercial infrastructure

South Plainfield, New Jersey

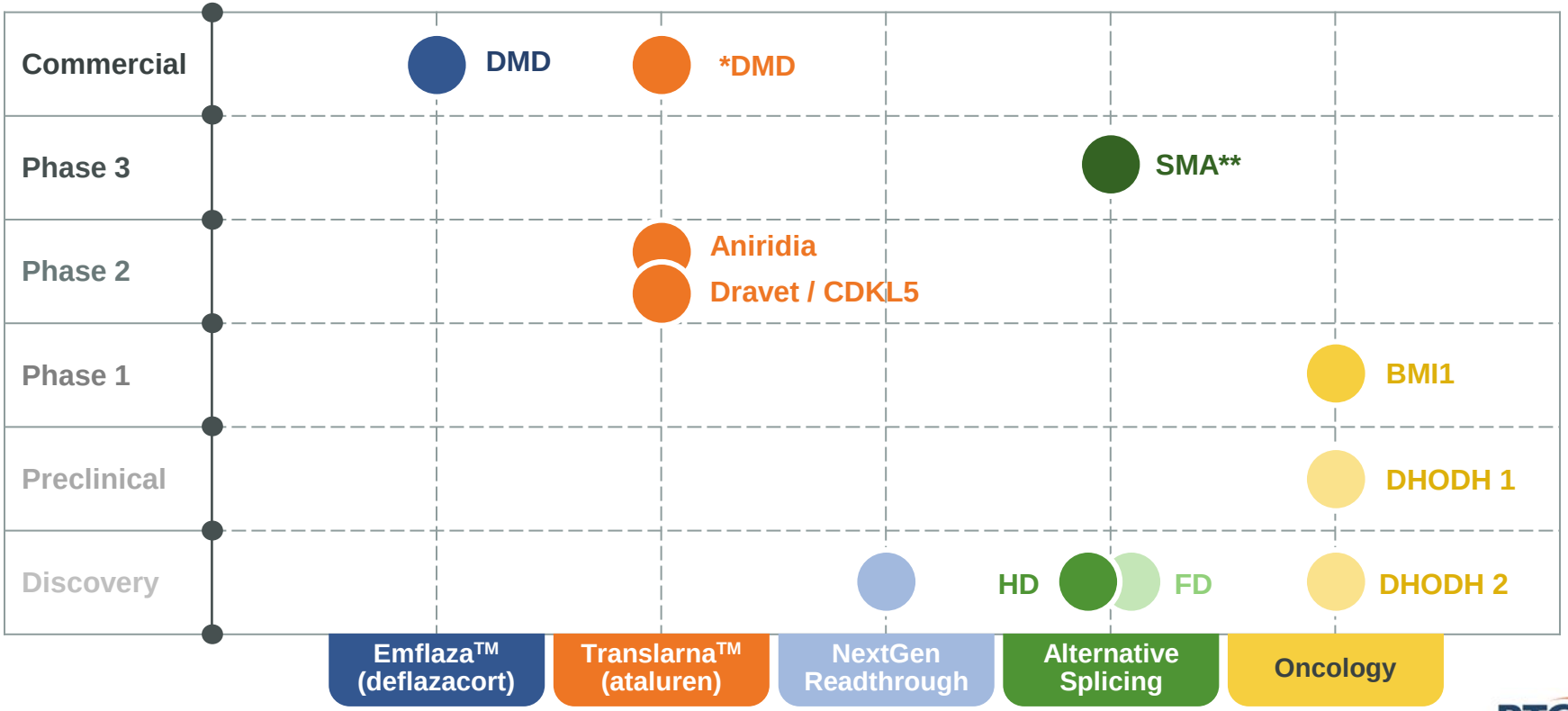
Zug Switzerland, Marketing, Medical and Regulatory Hub



Dublin, Ireland International HQ

Latam Regional Office, Sao Paulo, Brazil

Expanding pipeline through in-house innovation



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

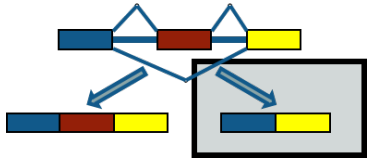
** Phase 3 Sunfish clinical study of RG7916 in SMA type 2/3 patients began in Nov 2016, Firefish pivotal stage in SMA type 1 patients to begin in coming months

Small molecule splicing technology

Broad platform addressing rare disorders

The spinal muscular atrophy program validates PTC's small molecule splicing platform

Splicing



Target splicing event to restore or reduce protein

SMA – SMN2
FD – IKBKAP
HD – HTT

RESEARCH | REPORTS

MOTOR NEURON DISEASE

SMN2 splicing modifiers improve motor function and longevity in mice with spinal muscular atrophy

Nikolai A. Naryshkin,[1] Maria Weetall,[1] Amal Dakka,[1] Jana Narasimhan,[1] Xin Zhao,[1] Zhihua Feng,[2] Karen E. Y. Ling,[2] Gary M. Karp,[1] Hongyan Qi,[1] Matthew C. Woll,[1] Guangming Chen,[1] Naxing Zhang,[1] Vijayalakshmi Gabbeta,[1] Priya Vazirani,[1] Anuradha Bhattacharyya,[1] Russell Furdon,[1] Nicole Richer,[1] Josephine Sheedy,[1] Ronald Kong,[1] Jiyuan Ma,[1] Anthony Turpoff,[1] Chang Sun Lee,[1] Xiaoyun Zhang,[1] Young Chun Moon,[1] Pamyatsa Tetiblin,[1] Elise M. Welch,[1] Joseph M. Colacino,[1] John Babiak,[1] Neil G. Almstead,[1] Stuart W. Peltz,[1] Frank A. Rigo,[1] Karen S. Chen,[1] Jesse L. Moll,[1] Maureen S. Lynes,[1] Lee L. Rubin,[2] Paolo Bonfanti,[2] Tina Santarelli,[2] Daniel Hurlstone,[2] Richard D. McCarthy,[2] Roland Schmucki,[2] Martin Ebeling,[2] Shanawani Sivasamaiyahnan,[3] China-Ping Ko,[3] Sergiy V. Panchkin,[3] Hanane Hatzi,[3] Irene Beltsch,[3] Antrean Ghosh,[3] Friedrich Metzger[2]*

Spinal muscular atrophy (SMA) is a genetic disease caused by mutation or deletion of the survival of motor neuron 1 (*SMN1*) gene. A paralogous gene in humans, *SMN2*, produces insufficient levels of functional SMN protein due to a mutation splicing that truncates the transcript. The decreased levels of SMN protein lead to progressive neuromuscular degeneration and high rates of mortality. Through chemical screening and optimization, we identified orally available small molecules that shift the balance of *SMN2* splicing toward the production of full-length *SMN2* messenger RNA with high specificity. Administration of these compounds to *SMN2* mice, a model of severe SMA, led to an increase in SMN protein levels, improvement of motor function, and protection of the neuromuscular circuit. These compounds also extended the lifespan of the mice. Selective *SMN2* splicing modifiers may have therapeutic potential for patients with SMA.

"The combination of structural and morphing capabilities that enhances or alters a particular material characteristic is likely where the most innovative applications of origami engineering lie."

MOLECULAR BIOLOGY

A splicing magic bullet

Drugs that modulate RNA splicing are potential

NEUROMUSCULAR DISORDERS

Beefing up the right splice variant to treat spinal muscular atrophy

Spinal muscular atrophy (SMA), the leading genetic cause of infant mortality, is characterized by progressive degeneration of motor neurons in the anterior horn of the spinal cord and atrophy of skeletal muscles. SMA results from mutations in survival of motor neuron 1 (*SMN1*). Naryshkin *et al.* have now identified orally available small-molecule compounds that alter the splicing of the nearly identical *SMN2*, which can improve motor function and extend lifespan in mouse models of SMA.

compounds that alter *SMN2* splicing thereby increasing the production of full-length *SMN2* transcripts. By screening a library of ~200,000 compounds and performing further chemical optimization for molecules that increase the ratio of full-length to Δ7 *SMN2* mRNA, they found three compound series — exemplified by compounds named SMN-C1, SMN-C2 and SMN-C3 — that increased the fraction of *SMN2* mRNAs that contain exon 7.

These compounds were then tested in two cell types from patients

The NEW ENGLAND JOURNAL of MEDICINE

CLINICAL IMPLICATIONS OF BASIC RESEARCH

Elizabeth G. Phimister, Ph.D., *Editor*

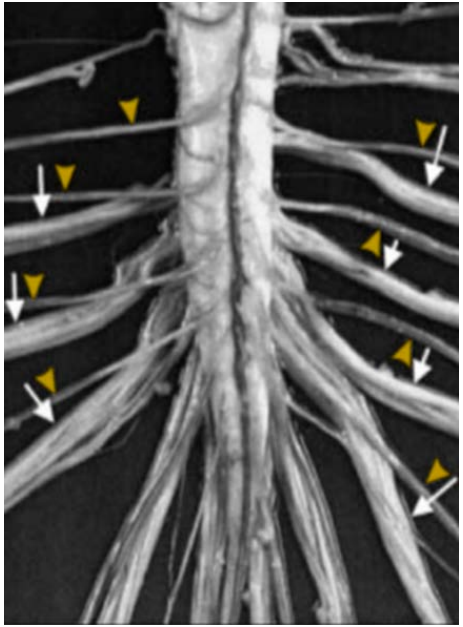
Romancing the Spliceosome to Fight Spinal Muscular Atrophy

Kathryn J. Swoboda, M.D.

Every scientist, clinician, and patient seeks that holy grail that will cure disease. Nowhere is this need more acute than in the field of neurodegeneration. In neurogenetic diseases, in the large majority of cases, aberrant code is embedded in the DNA in every cell, and the blood–brain barrier

cies from a single pre-mRNA template. Alternative splicing results in the exclusion of one or more exons from the mature mRNA and facilitates the expression of different protein isoforms (all derived from the same gene) at different stages of development, in different tissues, and in

Spinal Muscular Atrophy:
The leading genetic cause of mortality in infants

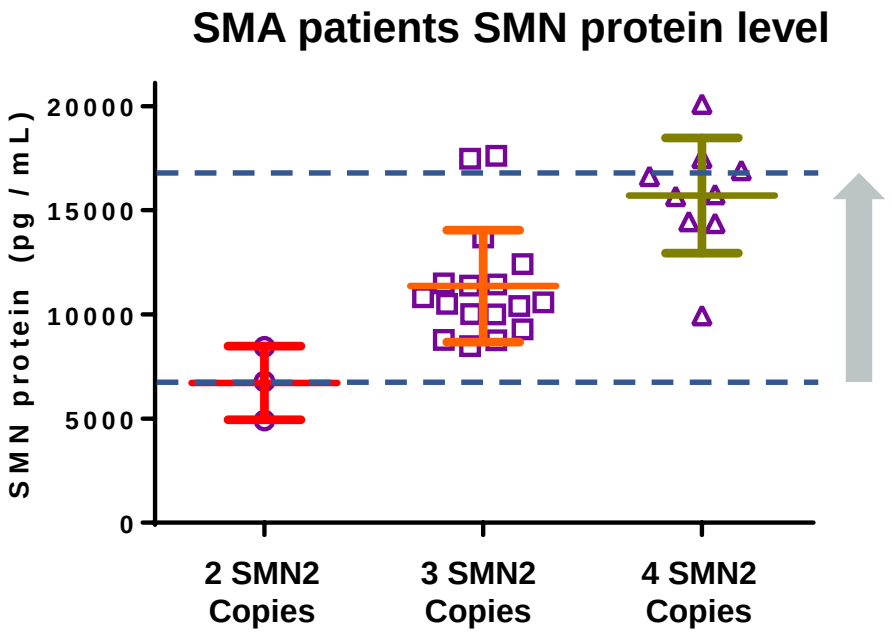


⇨ Dorsal Root
► Ventral Root

- Spinal muscular atrophy (SMA) is caused by the loss of SMN1 gene
- Low expression of SMN protein leads to the loss of motor neurons in the spinal cord
- One in every 10,000 children born is affected with the disorder
- Publications demonstrate involvement of muscle, liver, bones and other peripheral tissues in addition to CNS
- SMA program partnered with Roche and the SMA Foundation

RG7916 has the opportunity to be best in class

- Demonstrated complete restoration of SMN RNA in SMA patients
- RG7916 has shown 2.5 fold median increase in protein in patients
- Small molecule has potential for broad tissue distribution key to SMA treatment
- Oral administration



RG7916 has been well tolerated with no drug related safety findings leading to withdrawals

Advancing towards registration of RG7916

SUNFISH

- Clinical study in SMA type 2/3 patients between 2 and 25 years old
  - Ongoing pivotal part will enroll 168 patients, placebo controlled 2:1, endpoint of total motor function measure (MFM-32) at 12 months

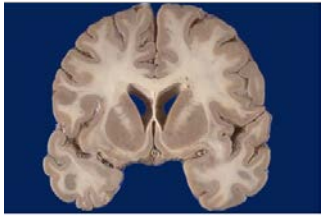
FIREFISH

- Clinical study in SMA type 1 patients between 1 and 7 months old
  - Open label study, completing dose finding part
  - Pivotal part expected to start in coming months, will enroll 40 babies, complete enrollment during 2018
  - Endpoint of sitting unsupported as measured by Bayley infant scales

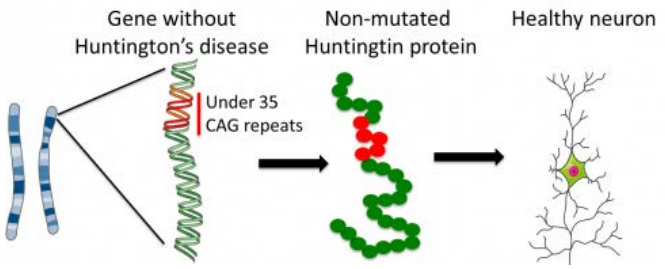
Firefish dose escalation survival data expected at EU SMA congress

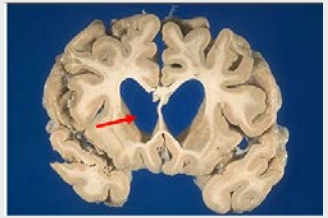
Huntington's Disease is caused by a CAG repeat expansion in the HTT gene

- HD is caused by expression of mutant Huntingtin (HTT) protein due to the CAG repeat expansion
- Neuron degeneration predominantly in the striatum and cerebral cortex
- High unmet medical need:
  - No approved disease modifying treatment

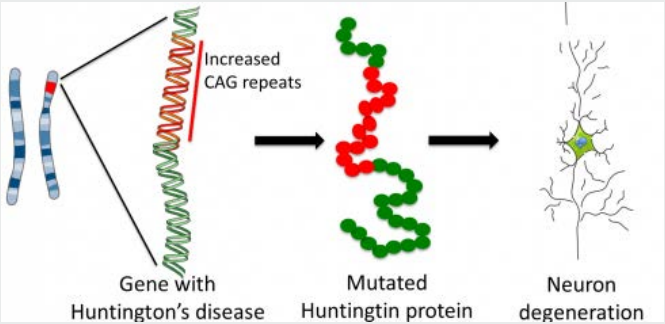


Healthy brain

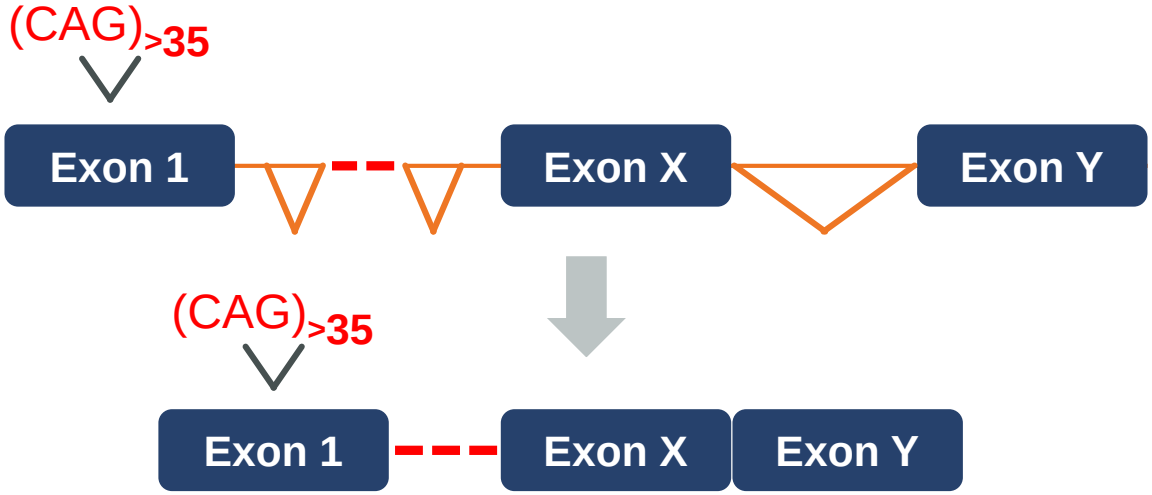


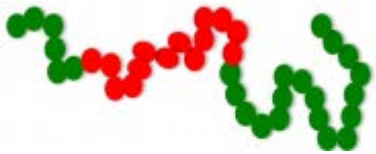


HD brain



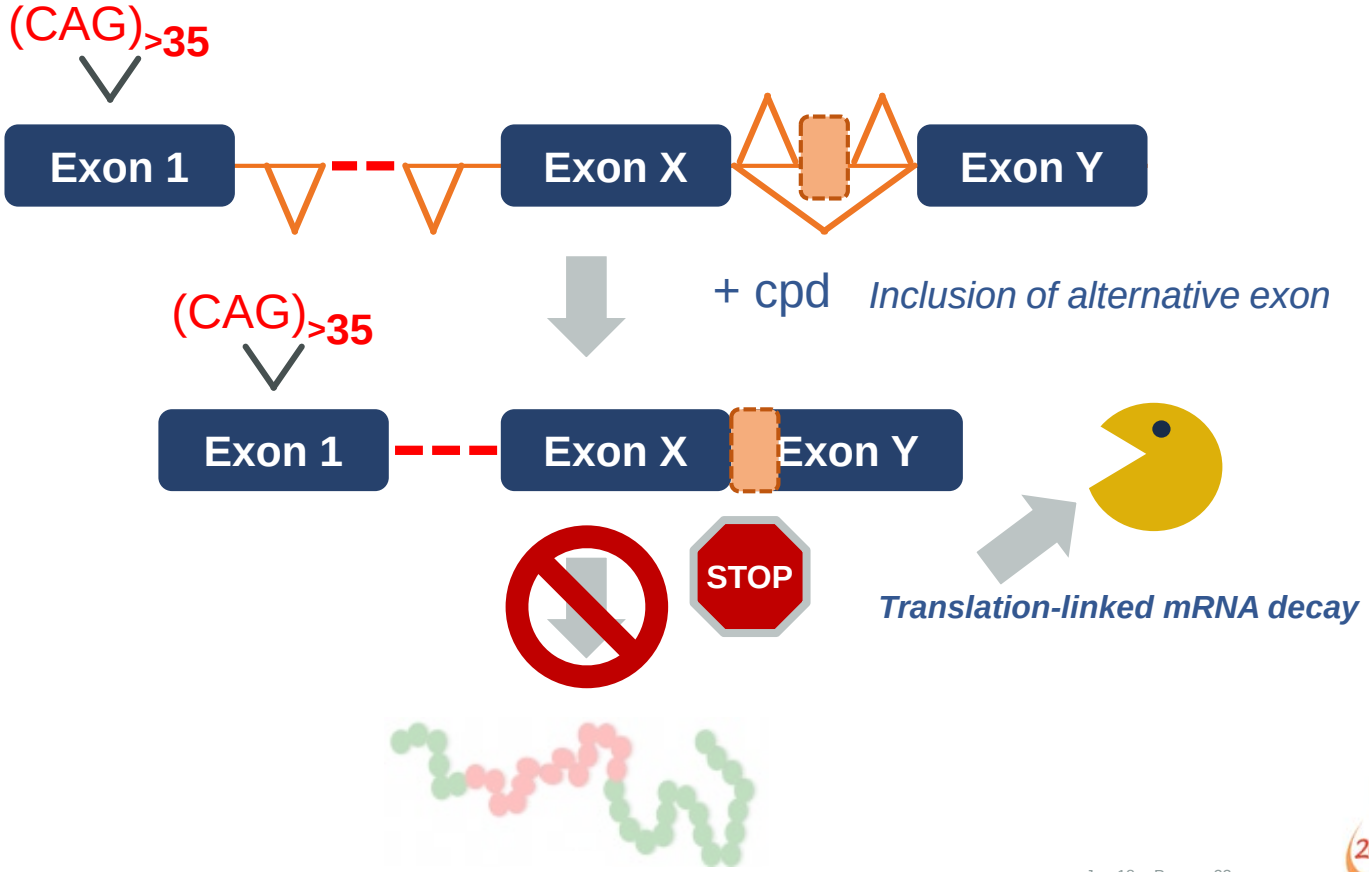
Treating HD by modifying HTT splicing





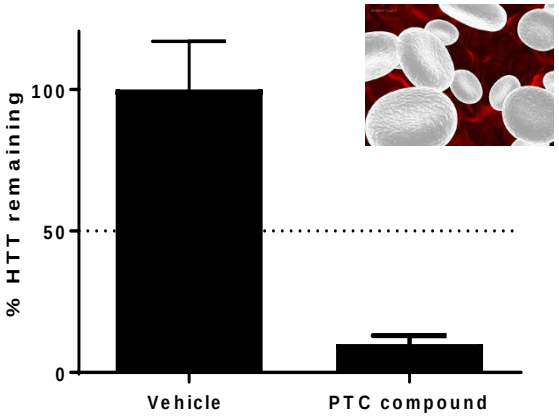
Mutant toxic
HTT protein

Opportunity to address HTT by leveraging PTC's splicing platform

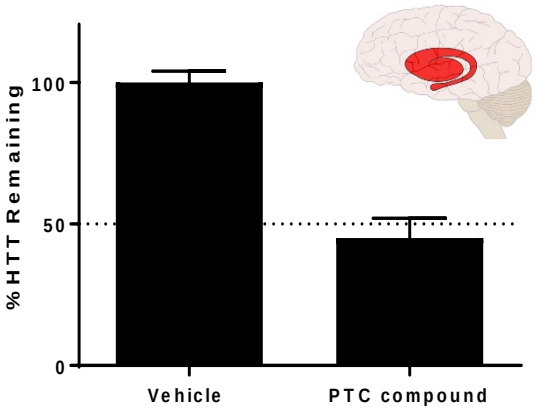


PTC compounds lower human HTT in key regions of the brain and tissues in a mouse model of HD

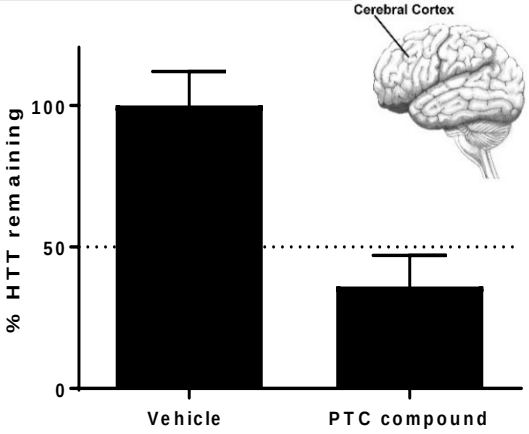
White blood cells



Striatum



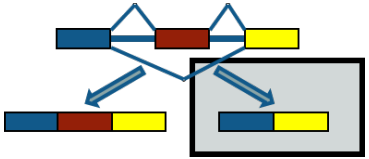
Cortex



Optimization has led to the discovery of several classes of small molecules

- ✓ Potent and selective to lowering of HTT mRNA and protein
- ✓ Widely distributed in animals, demonstrating HTT protein lowering in the brain and periphery

PTC's platform technologies target RNA biology to modulate gene expression with small molecules

Platform		Mechanism Targeted	Programs
Splicing		Target splicing event to restore or reduce protein	SMA – SMN2 FD – IKBKAP HD – HTT

- 20 years of targeting RNA biology for drug discovery and development
- Cutting edge platform technology discovered and developed by PTC
- Advancement of SMA program in pivotal clinical trials
- Several splicing-targeting programs amendable to several targets
  - Currently targeting HD, FD, and others

PTC: Discovering, developing and commercializing clinically differentiated therapies for rare disease

PTC's future events and milestones

SMA RG7916 data at EU SMA

U.S. FDA Translarna™ decision

Analyst Day highlighting pipeline

Establish Emflaza™ as U.S. DMD standard of care

15% CAGR Translarna revenue through 2022

Sustainable, growing DMD business enables continued innovation & growth

Total 2017 unaudited revenue of ~$195 million

1) Growing global DMD franchise with unaudited 2017 revenue of $174 million

($ million)	2017 Unaudited Revenue	2018 Financial Guidance
Translarna	$145	$170 - $185
Emflaza	$29	$90 - $110
DMD Franchise	**$174**	**$260 - $295**

2) Strong sustainable financial position

- 2018 GAAP R&D + SG&A $280-$290M
- 2018 non-GAAP R&D +SG&A $250 - $260 million (excludes $30M non-cash stock-based compensation expense)
- 12/31/17 cash position of ~$191

3) Pursuing internal and in-licensing value-creation opportunities

- Leverage our strong global commercial infrastructure