UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 6-K

REPORT OF FOREIGN PRIVATE ISSUER
PURSUANT TO SECTION 13a-16 OR 15d-16
UNDER THE SECURITIES EXCHANGE ACT OF 1934

For the month of June, 2019

Commission File Number: 001-36815

Ascendis Pharma A/S
(Exact Name of Registrant as Specified in Its Charter)

Tuborg Boulevard 12
DK-2900 Hellerup
Denmark
(Address of principal executive offices)

Indicate by check mark whether the registrant files or will file annual reports under cover of Form 20-F or Form 40-F.

Form 20-F ☒ Form 40-F ☐

Indicate by check mark if the registrant is submitting the Form 6-K in paper as permitted by Regulation S-T Rule 101(b)(1): ☐

Indicate by check mark if the registrant is submitting the Form 6-K in paper as permitted by Regulation S-T Rule 101(b)(7): ☐

On June 26, 2019, the presentations attached hereto as Exhibit 99.1 will be presented at an R&D Day held by Ascendis Pharma A/S (the "Company") in New York City.

The furnishing of the attached presentation is not an admission as to the materiality of any information therein. The information contained in the presentation is summary information that is intended to be considered in the context of more complete information included in the Company's filings with the Securities and Exchange Commission (the "SEC") and other public announcements that the Company has made and may make from time to time by press release or otherwise. The Company undertakes no duty or obligation to update or revise the information contained in this report, although it may do so from time to time as its management believes is appropriate. Any such updating may be made through the filing or furnishing of other reports or documents with the SEC, through press releases or through other public disclosures.

Exhibits

Exhibit No.	Description
99.1	R&D Day Presentations.

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Ascendis Pharma A/S

Date: June 26, 2019

By: /s/ Michael Wolff Jensen
Michael Wolff Jensen
Chairman and Senior Vice President, Chief Legal Officer

ascendis pharma

Ascendis Pharma A/S

R&D Day

June 26, 2019

Cautionary Note On Forward-Looking Statements

This presentation contains forward-looking statements. All statements other than statements of historical facts contained in this presentation, such as statements regarding our future results of operations and financial position, including our business strategy, prospective products, availability of funding, clinical trial results, product approvals and regulatory pathways, collaborations, timing and likelihood of success, plans and objectives of management for future operations, and future results of current and anticipated products, are forward-looking statements. These forward-looking statements are based on our current expectations and beliefs, as well as assumptions concerning future events. These statements involve known and unknown risks, uncertainties and other factors that could cause our actual results to differ materially from the results discussed in the forward-looking statements. These risks, uncertainties and other factors are more fully described in our reports filed with or submitted to the Securities and Exchange Commission, including, without limitation, our most recent Annual Report on Form 20-F filed with the SEC on April 3, 2019 particularly in the sections titled "Risk Factors" and "Management's Discussion and Analysis of Financial Condition and Results of Operations". In light of the significant uncertainties in our forward-looking statements, you should not place undue reliance on these statements or regard these statements as a representation or warranty by us or any other person that we will achieve our objectives and plans in any specified timeframe, or at all.

Any forward-looking statement made by us in this presentation speaks only as of the date of this presentation and represents our estimates and assumptions only as of the date of this presentation. Except as required by law, we assume no obligation to update these statements publicly, whether as a result of new information, future events or otherwise after the date of this presentation.

This presentation concerns product candidates that are or have been under clinical investigation and which have not yet been approved for marketing by the U.S. Food and Drug Administration, European Medicines Agency or other foreign regulatory authorities. These product candidates are currently limited by U.S. Federal law to investigational use, and no representations are made as to their safety or effectiveness for the purposes for which they are being investigated. These presentation materials include a presentation from Dr. Ezra Cohen, who is an expert in the field in which he is presenting. He is providing background information about certain diseases, but his views do not necessarily represent those of the Company.

Today's Agenda

9:00-9:05 a.m.	**Welcome & Agenda Overview** Scott T. Smith
9:05-9:15 a.m.	**Vision 3x3** Jan Møller Mikkelsen
9:15-9:30 a.m.	**TransCon Platform & Product Innovation** Kennett Sprogøe, Ph.D.
9:30-10:05 a.m.	**TransCon hGH** Jonathan Leff, M.D.
10:05-10:15 a.m.	**Connected Healthcare Platform** Thomas Ørts Pedersen
10:15-10:30 a.m.	**Commercialization Update** Tom Larson
10:30-10:40 a.m.	**Q&A: TransCon hGH**
10:40-10:50 a.m.	**Break**
10:50-11:20 a.m.	**TransCon PTH** David Karpf, M.D. & Nyssa Liebermann Noyola
11:20-11:35 a.m.	**TransCon CNP** Kennett Sprogøe, Ph.D.
11:35-11:45 a.m.	**Q&A: TransCon PTH & TransCon CNP**
11:45-12:05 p.m.	**Introducing Oncology** Jan Møller Mikkelsen & Juha Punnonen, M.D., Ph.D.
12:05-12:20 p.m.	**IO & IT Treatments: Challenges & Promise** Ezra Cohen, M.D.
12:20-12:40 p.m.	**Oncology Product Candidates** Juha Punnonen, M.D., Ph.D.
12:40-12:50 p.m.	**Q&A: Oncology**
12:50-1:00 p.m.	**General Q&A & Closing Remarks** Jan Møller Mikkelsen

ascendis pharma

Vision 3x3

Jan Mikkelsen
President & CEO

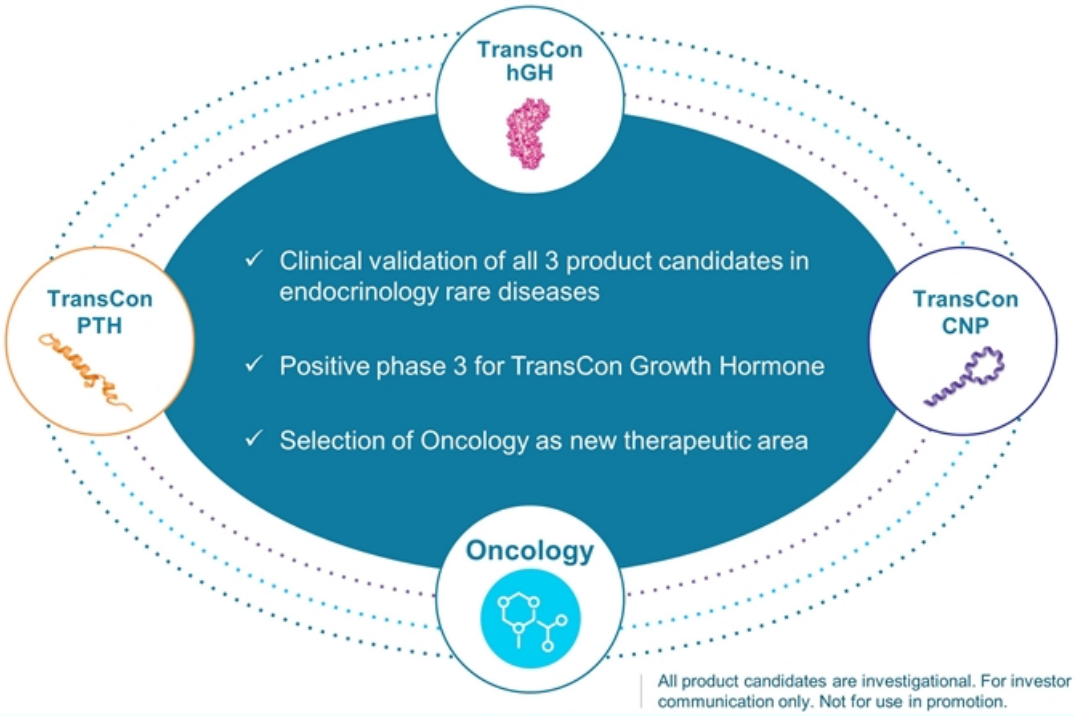
Building a Leading Rare Disease Company

Slide presented at R&D Day 2016

- Leverage the validated TransCon technology to create best-in-class products
- Advance the company's pipeline of three rare disease endocrinology product candidates:
  - Phase 3 ongoing for TransCon Growth Hormone
  - File INDs for TransCon PTH and TransCon CNP in 2017
  - Obtain approval for at least two products between 2020-2024
- Next rare disease therapeutic area to come
  - Identify clinical stage candidate by 2020
- Build an integrated commercial business focused on the U.S. market

ascendis pharma

Vision 20/20: Established the Foundation for a Leading Rare Disease Company



Vision 3x3: Building a Leading BioPharma Company

Our Goal is to Achieve Sustainable Growth through Multiple Approaches

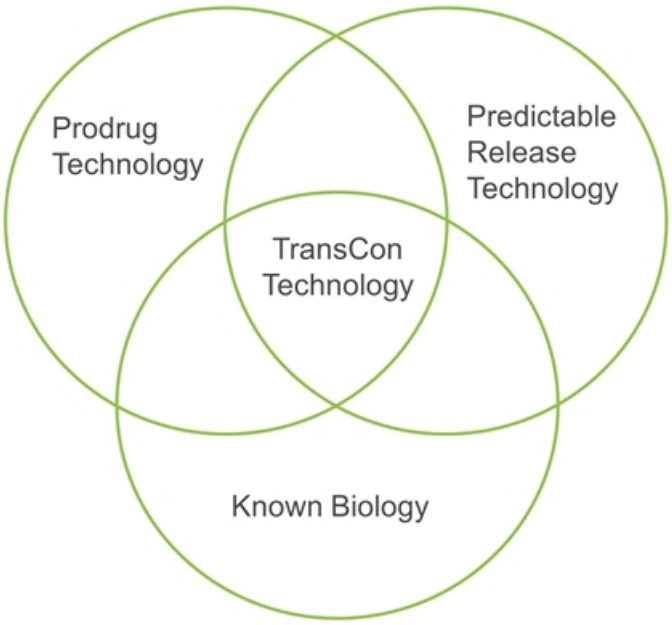
- Obtain regulatory approval for 3 Endocrinology Rare Disease products
  - TransCon hGH for pediatric growth hormone deficiency
  - TransCon PTH for adult hypoparathyroidism
  - TransCon CNP for achondroplasia
- Growth of Endocrinology Rare Disease pipeline through:
  - Label expansion programs with the goal of obtaining 9 indications in total
  - Global clinical reach directly or through partnerships
- Build an integrated commercial business for our Endocrinology Rare Disease franchise in North America and select European countries
  - Establish global commercial presence with partners outside our geographic areas
- Create 3 independent therapeutic areas each with a diversified pipeline built on TransCon technologies and our unique algorithm for product innovation
  - Established oncology as next independent therapeutic area

ascendis pharma

TransCon™ Technology Platform & Product Innovation

Kennett Sprogøe, Ph.D.
SVP, Head of Innovation and Research

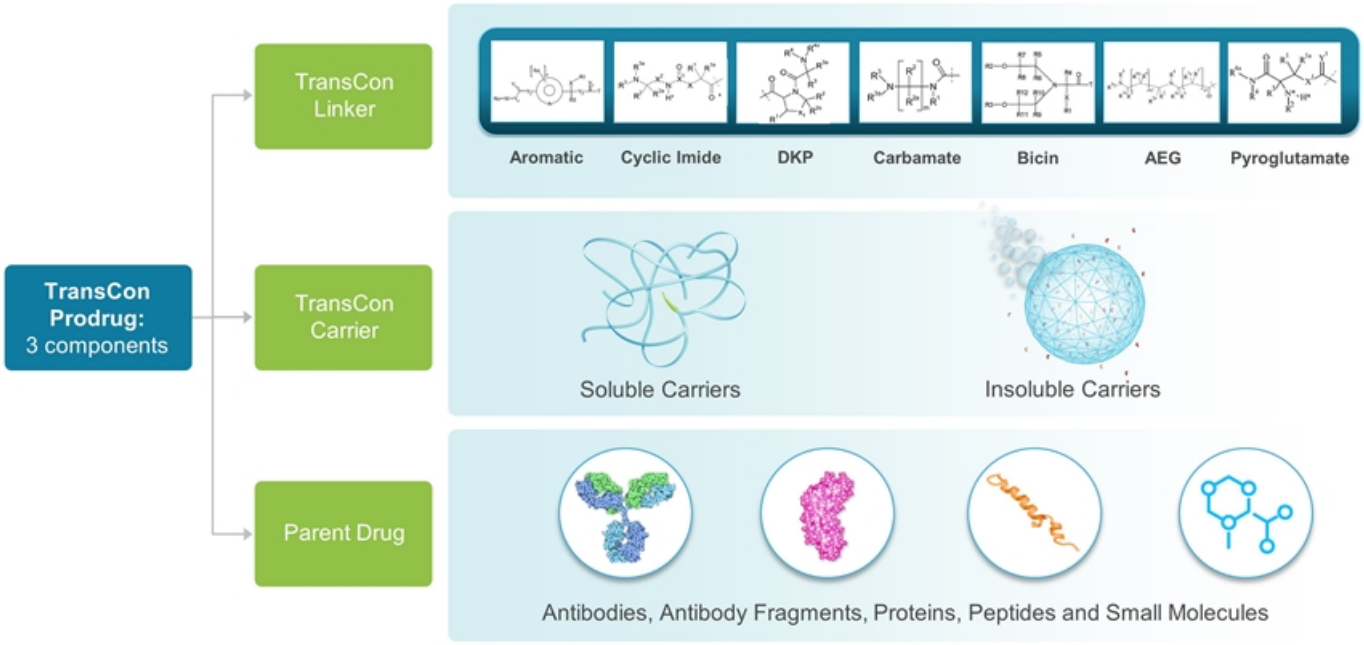
TransCon Technology: A Combination of Technologies



TransCon combines the benefits of Prodrug and Predictable Release Technologies with Known Biology to create highly differentiated products for the benefit of patients

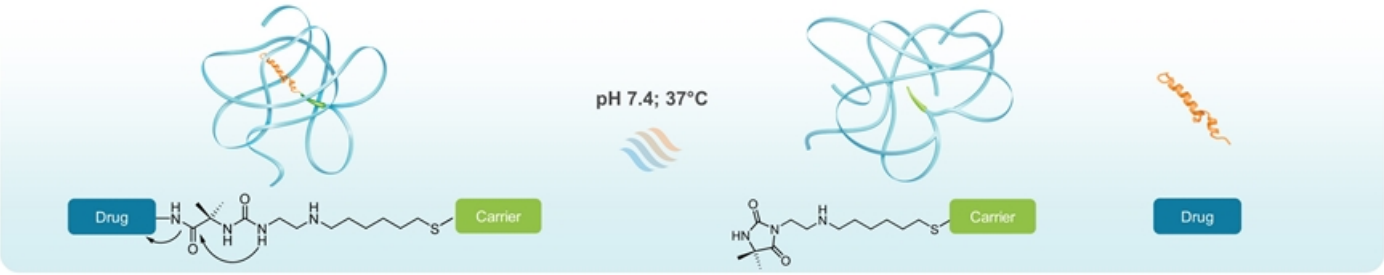
ascendis pharma

*Trans*ient *Con*jugation: Flexible and Versatile Platform



TransCon Technology: The TransCon Linker

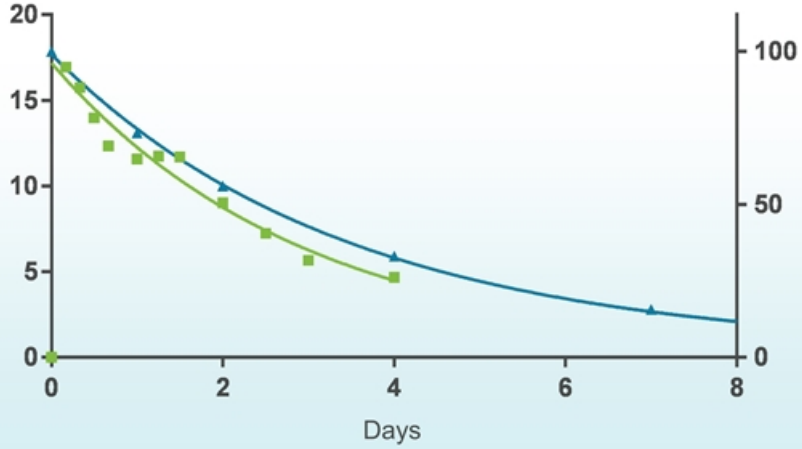
- Cleaves in an enzyme-independent fashion, ensuring reproducible drug release; *in vitro* to *in vivo* correlation with high predictability
- TransCon linkers remain covalently bound to the carrier molecule after release of the unmodified parent drug
- Enables tunable design of prodrugs with dosing frequency from daily up to six months or more



TransCon Drug Release is Predictable

In vivo
TransCon PTH phase 1 interim data [124 µg dose]

Free PTH [pg/mL]



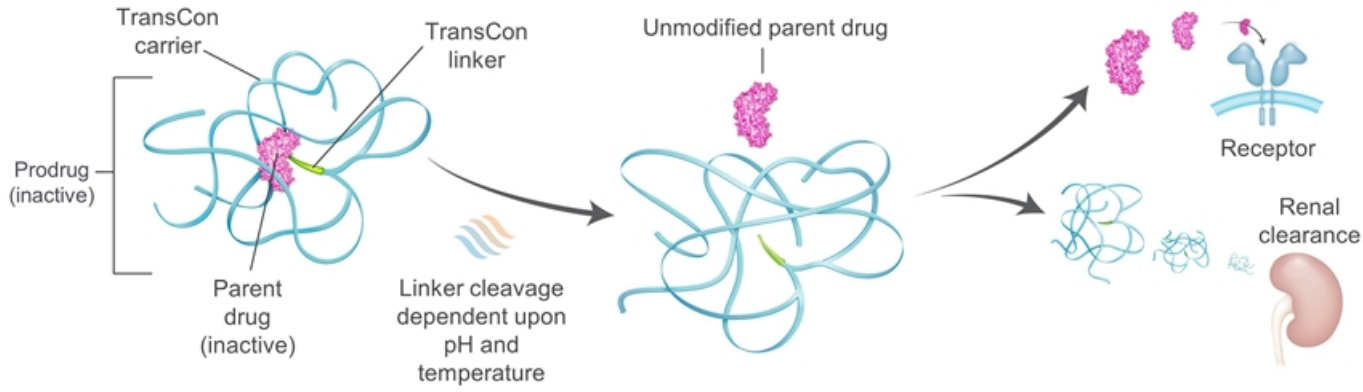
In vitro
TransCon PTH release kinetics at pH 7.4 and 37°C

Residual peptide [%]

High predictability of PK profile from *in vitro* data enables optimization of PK profile of lead candidates *in vitro* prior to initiating *in vivo* development

ascendis pharma

TransCon Technology: Sustained Systemic Delivery

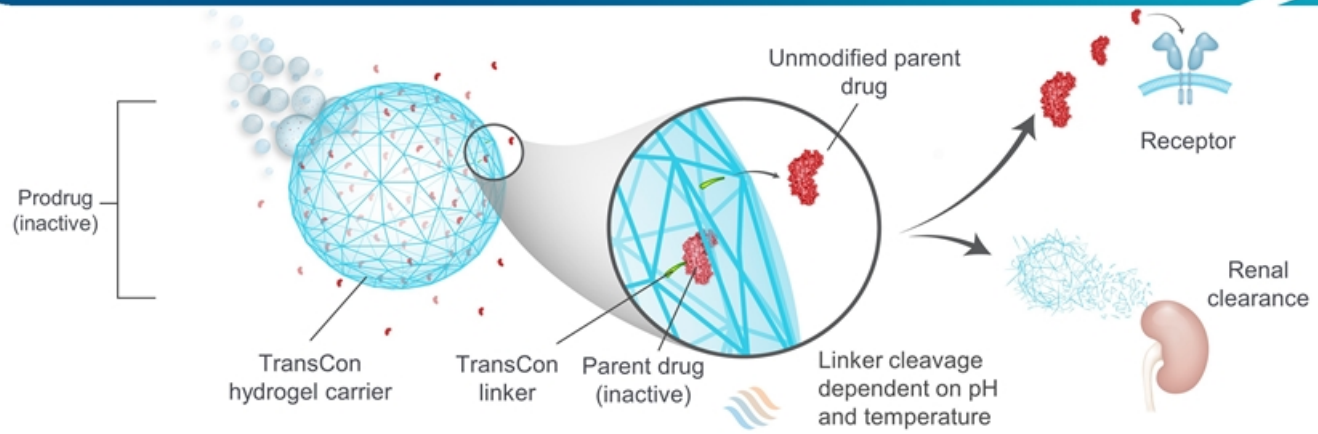


Parent drug is transiently bound to a TransCon linker-soluble carrier moiety, which inactivates and shields parent drug from clearance

Following injection, the linker is designed to autocleave at a specific rate to predictably release unmodified parent drug

Designed to distribute released drug like the parent molecule; linker-carrier is cleared renally

TransCon Technology: Sustained Localized Delivery



Parent drug is transiently bound to TransCon linker-hydrogel carrier, which inactivates, shields parent drug and prevents clearance

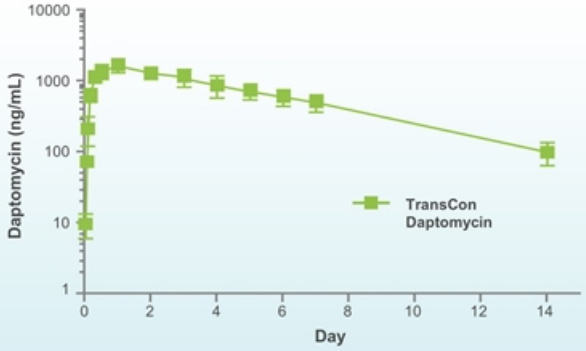
Following injection, the linker is designed to autocleave at a specific rate to predictably release unmodified parent drug

Designed to provide sustained high local drug levels with low systemic exposure; hydrogel degrades into small polymers that are renally cleared

Sustained Localized Delivery: Validated Across Multiple Drugs and Administration Sites

Small Molecules

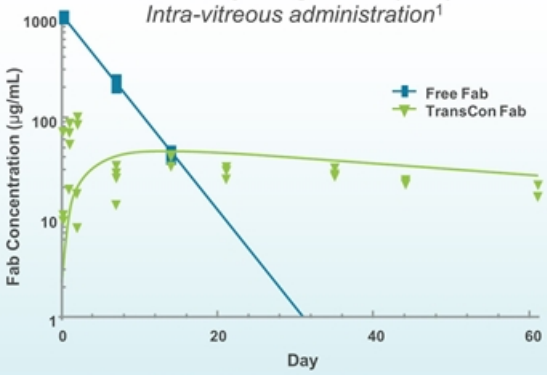
Intra-articular administration



Plasma PK of Daptomycin following intra-articular administration in rabbits. TransCon Daptomycin half-life was ~3 days.

Antibody Fragments (Fab)

Intra-vitreous administration[1]



Vitreal PK of Fab following intra-vitreous administration in rabbits. TransCon Fab half-life was ~53 days compared to free Fab half-life of ~3.2 days.

- Excellent local tolerability of TransCon hydrogel carrier
- Sustained high local concentration with low systemic exposure

[1] Patent WO2018175788

ascendis pharma

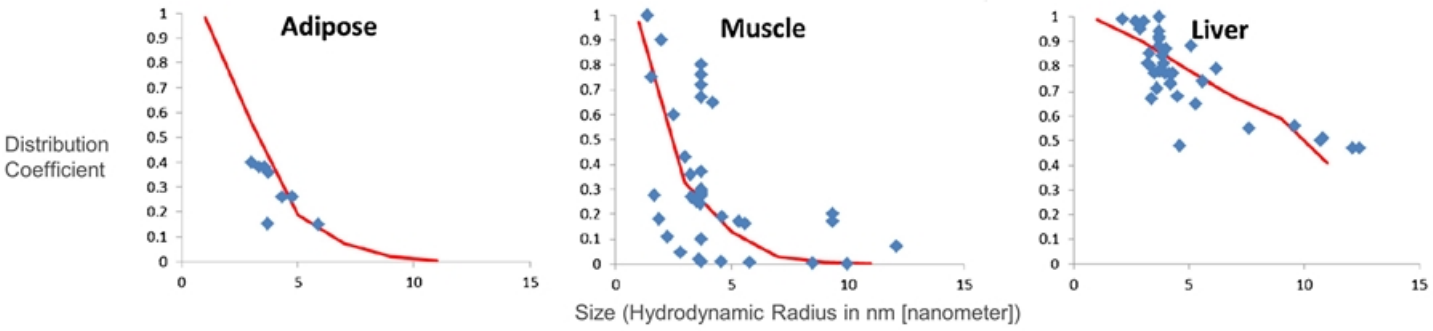
Why Size Matters: Releasing Unmodified Drug

A molecule's hemodynamic radius predicts tissue distribution[1]

- Albumin (66 kDa) is 3.6 nm, effectively maintaining a high albumin concentration in the blood compartment and low tissue concentrations
- hGH (22 kDa) is 2 nm, allowing distribution into adipose, muscle, brain and liver

The growth plate is avascular, representing a diffusion barrier

- Studies in mice suggest molecules 40 kDa and larger has restricted access to the growth plate[2]
- Relatively higher systemic drug concentrations are required to provide efficacious drug levels



[1] Anat Rec A; 2006, 288A: 91-103. [2] AAPS J. 2016, 18(1): 157-170.
kDa = kilodalton, a measure of weight

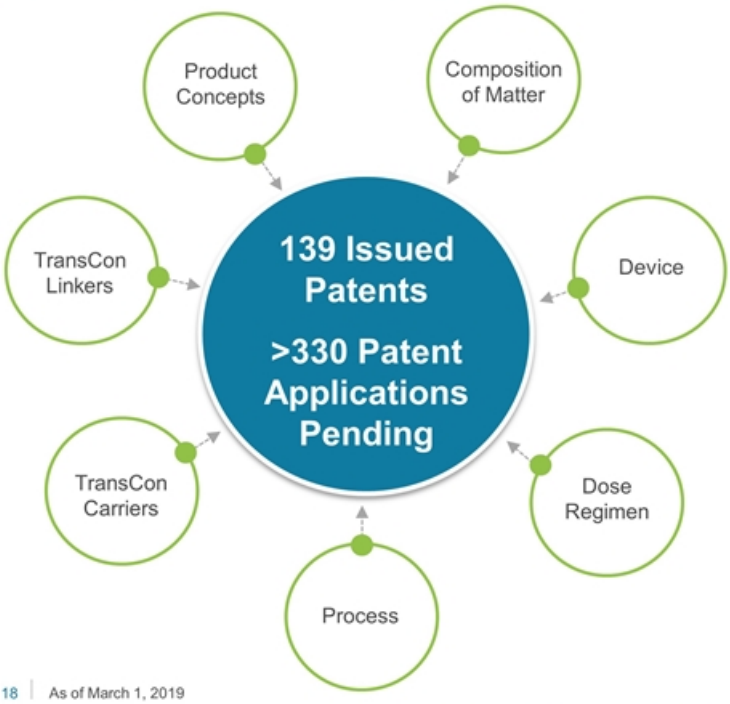
Ascendis Algorithm for Product Innovation

Our unique algorithm for product innovation has resulted in clinical validation of 3 out of 3 product candidates and positive phase 3 data in Endocrinology Rare Disease

We are continuing to apply our algorithm to build a pipeline in oncology and are committed to entering a 3rd therapeutic area

ascendis pharma

TransCon Enables Multi-level Patent Protection



- TransCon prodrugs eligible for new composition of matter IP
- A multi-layered patent strategy is applied to protect our assets

ascendis pharma

TransCon: A New Innovative Technology Platform

- TransCon technologies combine the benefits from prodrug and predictable release technologies with known biology – in one single platform
- TransCon prodrugs release unmodified drug expected to maintain the same mode of action as parent drug (receptor activation, distribution, etc.)
- Broad applicability for both systemic (s.c. / i.v.) and localized delivery (intravitreal, intratumoral, inhaled)
- Product features may include low injection volume, room temperature storage, small needle size (31G)
- Daily, weekly, monthly, or twice yearly or longer administration frequencies
- TransCon has a high success rate in endocrinology with clinical validation of 3 out of 3 product opportunities and positive phase 3 results for TransCon hGH

TransCon™ Growth Hormone: Once-Weekly Replacement Therapy

Jonathan A. Leff, M.D.
SVP, Chief Medical Officer

Growth Hormone Deficiency Is Not Just About Height: Growth Hormone Supports Overall Endocrine Health

BODY COMPOSITION

Increased fat mass, decreased muscle mass and decreased bone density can occur soon after treatment discontinuation.[2,3,4]

CARDIOVASCULAR DISEASE

Early discontinuation of GH treatment may induce impairment of patients' lipid profiles and cardiac function, leading to increased risk for CV disease.[6,7]

ULTIMATE HEIGHT ACHIEVEMENT

Children with GHD may not obtain full height potential if untreated.[1]

MENTAL HEALTH

A high incidence of psychiatric disorders, usually accompanied by poor life quality, is associated with adults who were GHD as children.[5]

FRACTURES

Adult peak bone mass is considerably lower, and rates of fractures are significantly higher among adults with GHD who were not treated as children.[8]

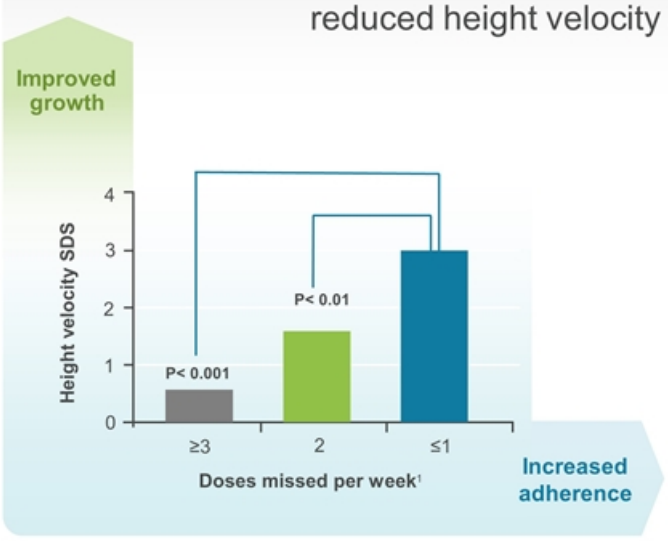
Daily hGH addresses all the symptoms of the disease; long-acting growth hormone products must fully mimic daily hGH to adequately address the totality of the disease

Sources: 1. de Boer, H. et al. 1997; 2. Rutherford, O. M. et al. 1991. 3. Colle, M., J. Auzerie.1993. 4. Johannsson, Gudmundur, et al. 1999. 5. Stabler, Brian et al. 1996. 6. Leong, Gary M., Gudmundur Johannsson. 2003. 7. Colao, Annamaria et al. 2002. 8. Bex, M, and R Bouillon. 2003

ascendis pharma

Daily Growth Hormone: The Problem

Poor adherence with daily hGH therapy is associated with reduced height velocity and impaired quality of life[1]



In the 1st year, two of three patients miss >1 injection on average per week[1]

Reduced frequency of administration is associated with better adherence[2]

[1] PLoS ONE 2011, 6(1): e16223
[2] Clinical Therapeutics 2008, 30(2): 307-316

A Decades-Long Pursuit: Long-Acting Growth Hormones[1]

Approaches

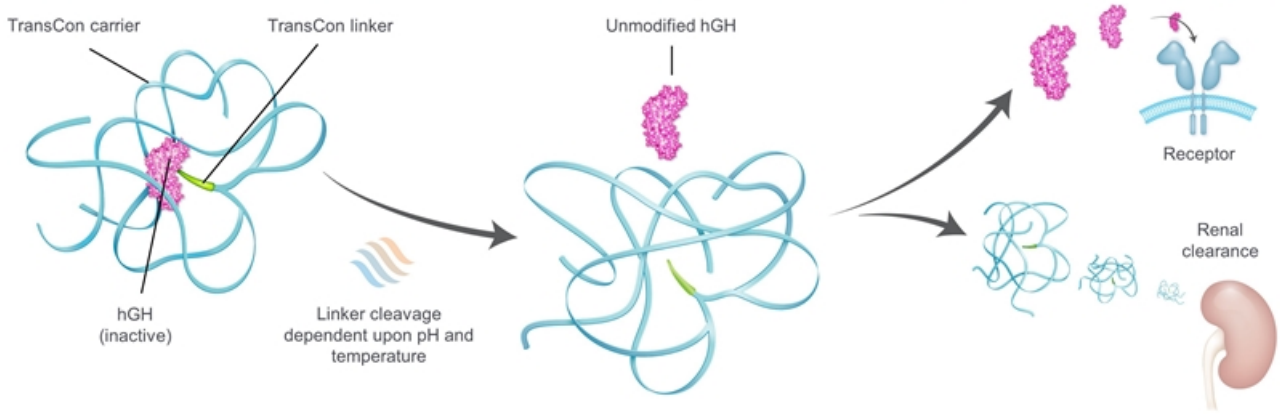
- Depot formulations
- PEGylated (permanent) formulations
- GH fusion proteins (molecular enlargement)
- Non-covalent albumin binding

Challenges

- Appropriate tissue penetration hindered by large size
- Immunogenicity (neutralizing antibodies)
- Viscous and painful formulations
- Large bore needle requirements
- Inadequate pharmacokinetics

[1] European Journal of Endocrinology (2016) 174, C1–C8

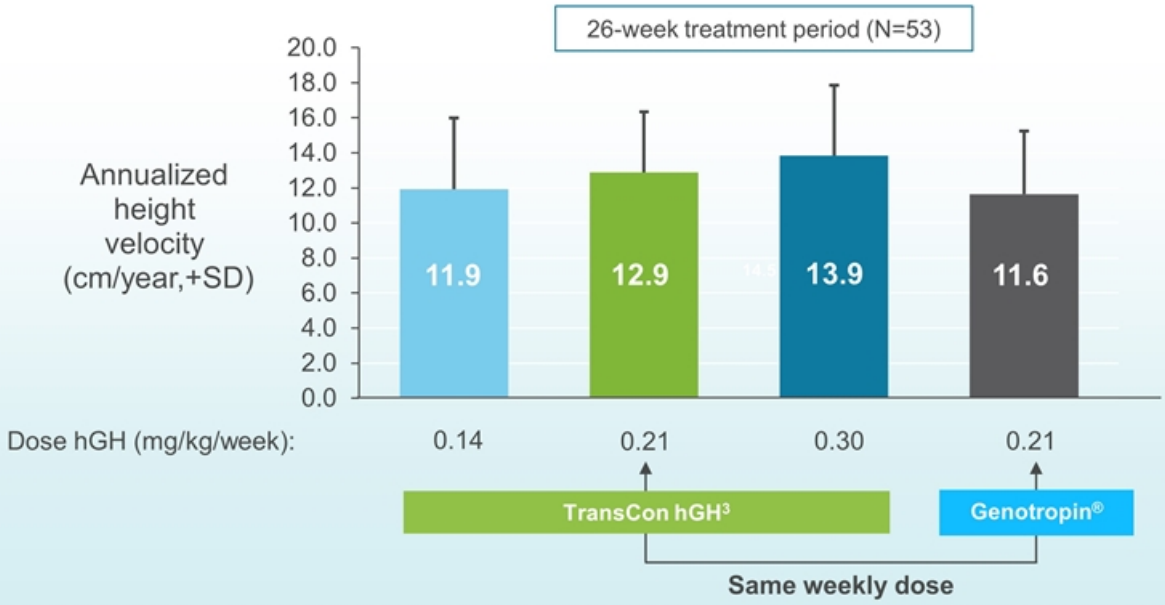
TransCon hGH Design



Once-weekly prodrug releases unmodified hGH designed to mimic daily hGH:

- ✓ Tissue distribution
- ✓ Physiological levels
- ✓ Therapeutic effects: efficacy, safety and tolerability

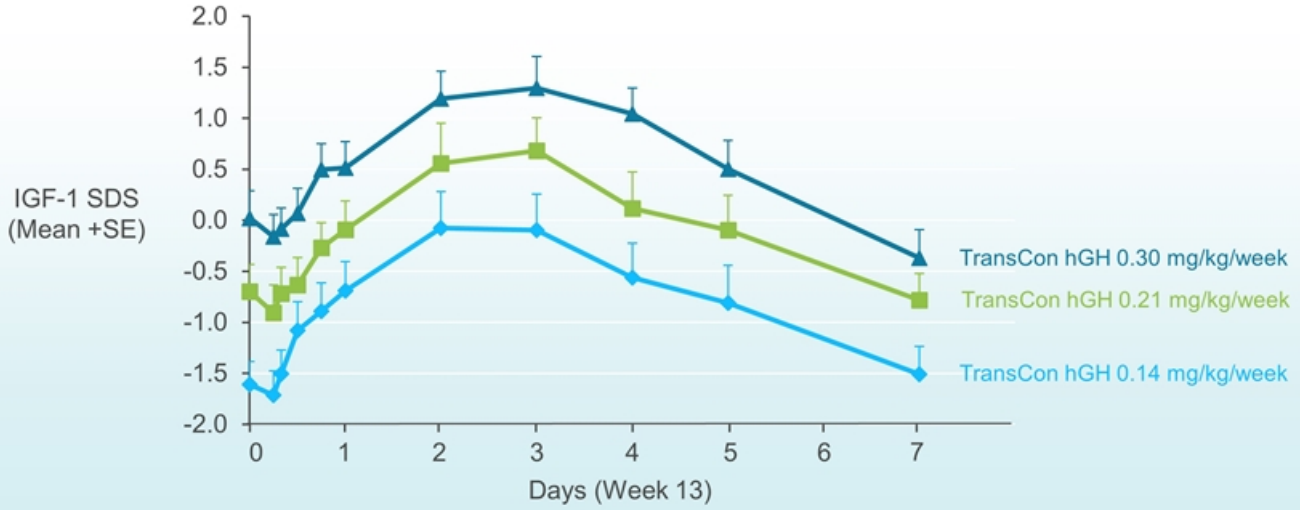
Growth Comparable to a Daily hGH in Phase 2[1,2]



[1] Intergroup differences not statistically significant
[2] J Clin Endocrinol Metab 2017, 102(5): 1673–1682
[3] Conducted with a bioequivalent version of TransCon hGH

ascendis pharma

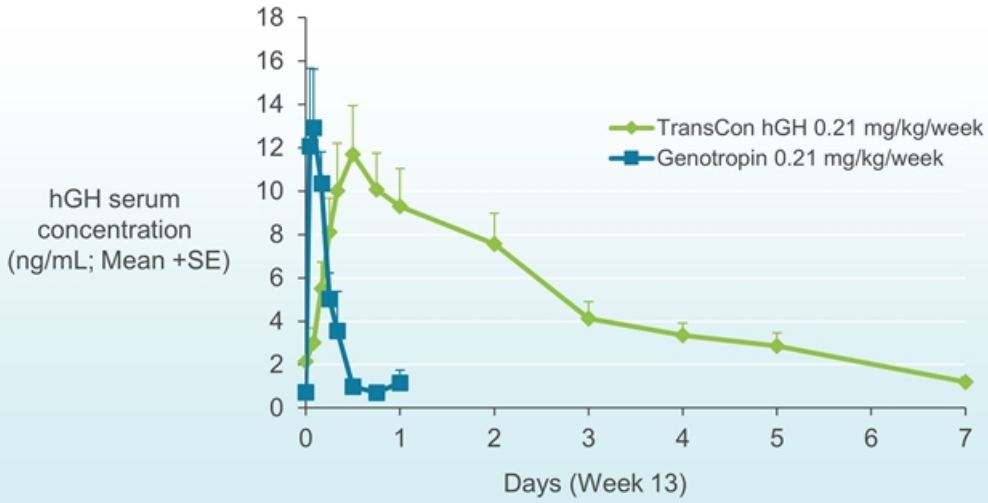
Dose Proportional IGF-1 Response in Phase 2[1]



Transient values > +2.0 observed in a small number of subjects, primarily at the highest dose level

[1] J Clin Endocrinol Metab 2017, 102(5): 1673–1682

Comparable hGH Levels in Phase 2[1]



Maximum hGH concentration comparable between equivalent weekly doses of TransCon hGH and a daily hGH

[1] J Clin Endocrinol Metab 2017, 102(5): 1673–1682

ascendis pharma

TransCon hGH Phase 3 Program in Pediatric GHD

N=161

- Treatment-naïve subjects
- Top-line data reported

N=146

- Subjects previously treated (n=143) and treatment-naïve (<3 years, n=3)
- Top-line data reported

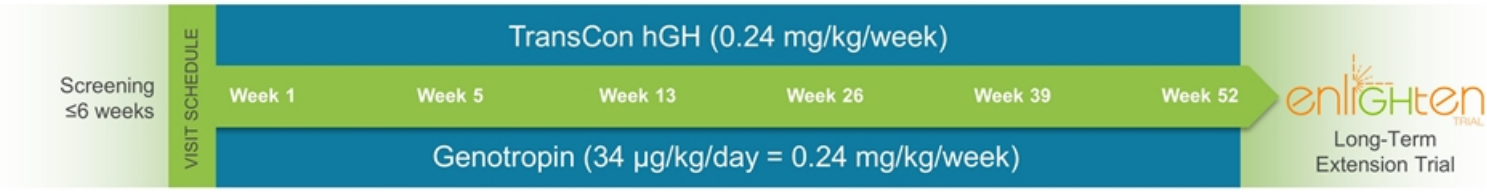
Extension trial (N=~300)

Regulatory filings (BLA H1 2020, MAA H2 2020)

Phase 3 heiGHt Trial

heIGHt TRIAL

161 treatment-naïve children with GHD dosed (2:1 randomization)



Objective

- Demonstrate non-inferiority

Key Inclusion Criteria

- Prepubertal children with GHD
- Height SDS ≤-2.0
- IGF-1 SDS ≤-1.0
- 2 GH stimulation tests (GH ≤10 ng/mL)
- Bone age ≥6 months behind chronological

Key Endpoints

- Annualized height velocity (HV) at 52 weeks (primary endpoint)
- Annualized HV at earlier time points
- Change in height SDS over 52 weeks
- Change in serum IGF-1/IGFBP-3 levels
- Change in IGF-1 SDS and IGFBP-3 SDS
- Normalization of IGF-1 SDS
- hGH and IGF-1 levels over 168 hours at Week 13 (PK/PD subset)

Demographics and Baseline Characteristics Comparable Between Arms

	TransCon hGH (n=105) Mean	Genotropin (n=56) Mean
Age (years)	8.51	8.48
Male (%)	81.9	82.1
Height SDS	-2.89	-3.00
Δ Average Parental Height SDS	-2.32	-2.55
IGF-1 SDS	-2.08	-1.96
Peak Stimulated GH (ng/mL)	5.89	5.48
BMI (kg/m^2)	16.1	16.5
BMI SDS	-0.32	-0.14
Bone Age (years)	5.84	5.98
Bone Age-to-Chronologic Age (BA/CA)	0.69	0.70
Caucasian (%)	95.2	92.9

Phase 3 heiGHt Trial Achieved Excellent Adherence[1]

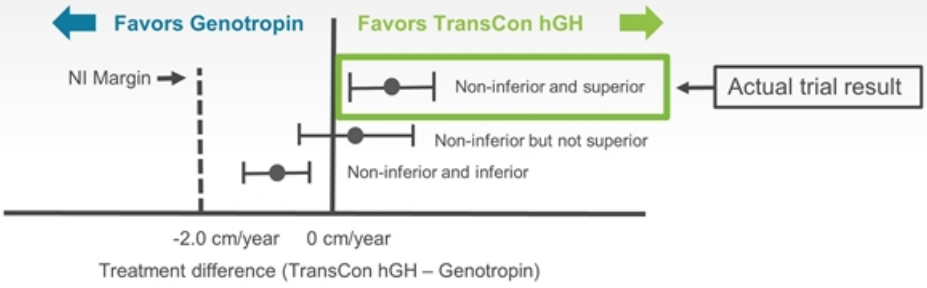
	TransCon hGH (n=105)	Genotropin (n=56)
Adherence Range, n (%)		
≤80%	0	1 (1.8)
>80% to ≤90%	0	0
>90% to ≤95%	1 (1.0)	2 (3.6)
>95% to ≤100%	104 (99.0)	53 (94.6)
Mean Adherence Rate, %	99.6	98.6

High level of adherence in both arms of the heiGHt Trial, as anticipated in well executed phase 3 trials

Adherence calculated as number of injections with study drug from baseline to final visit divided by 52 for TransCon hGH and 365 for Genotropin.
Top-line results from phase 3 heiGHt Trial.

TransCon hGH Met Primary Objective of Non-inferiority and Demonstrated Superiority in AHV at Week 52

	TransCon hGH (n=105)	Genotropin (n=56)	Estimate of Treatment Difference	P-value
LS Mean AHV at Week 52 (cm/year)	11.2	10.3	0.86	0.0088
Standard Error	0.23	0.30	0.33	
95% Confidence Interval (cm/year)	10.71 – 11.62	9.73 – 10.89	0.22 – 1.50	



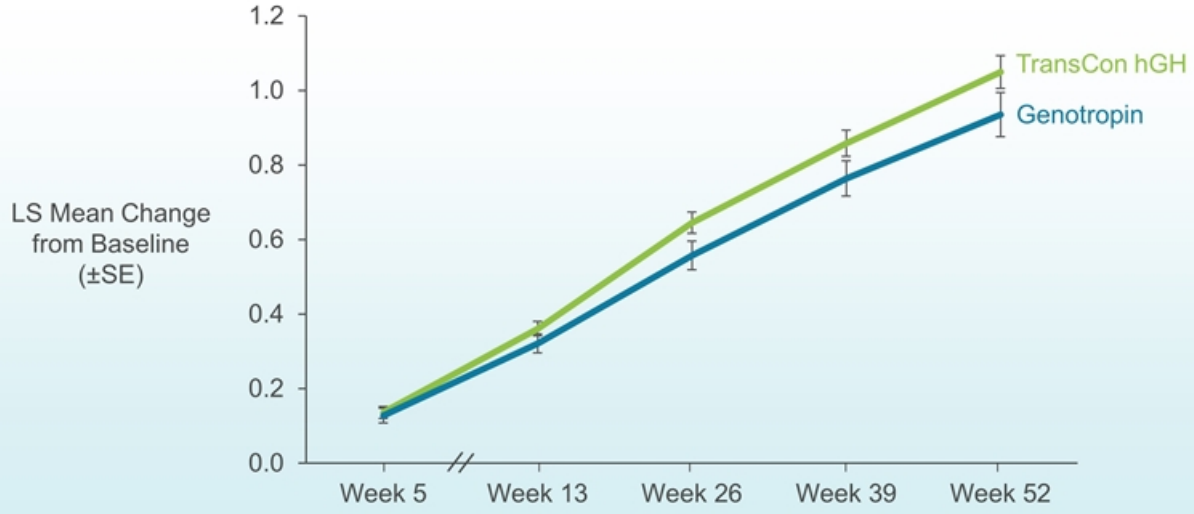
ANCOVA model was applied after missing data were imputed by multiple imputation method.
Top-line results from phase 3 heiGHt Trial.

AHV Reached Statistical Significance by Week 26

AHV by Visit (cm/year)	Estimated Difference LS Mean (SE)	[95% CI]	P-value
Week 5	0.7 (1.5)	[-2.3 – 3.7]	0.6402
Week 13	1.1 (0.7)	[-0.3 – 2.4]	0.1286
Week 26	1.4 (0.5)	[0.5 – 2.3]	**0.0017**
Week 39	1.0 (0.4)	[0.3 – 1.7]	**0.0061**
Week 52	0.9 (0.3)	[0.2 – 1.5]	**0.0088**

ANCOVA model was applied after missing data were imputed by multiple imputation method.
Top-line results from phase 3 heiGHt Trial.

Change in Height SDS Demonstrated an Increasing Difference



MMRM model.
Top-line results from phase 3 heiGHt Trial.

Mean AHV by Subgroups: TransCon hGH Performance Consistent Across Subgroups

	AHV at Week 52 (cm/year)	
	TransCon hGH (n=105) Arithmetic Mean	Genotropin (n=56) Arithmetic Mean
Age		
<6 years old	11.9	10.5
≥6 years old	10.6	10.1
Gender		
Male	10.7	10.0
Female	11.9	11.0
Peak Stimulated GH		
≤5 ng/mL	11.5	10.8
>5 ng/mL	10.6	9.9

AHV Poor Responders: Post-hoc Analysis

Poor responders defined as AHV <8.0 cm/year[1]

At Week 52[2]	TransCon hGH (n=104) n (%)	Genotropin (n=55) n (%)
Responder	100 (96.2)	49 (89.1)
Poor Responder	4 (3.8)	6 (10.9)

Incidence of poor responders ~3x lower in TransCon hGH arm compared to daily Genotropin arm

[1] Bakker et. al. *J Clin Endocrinol Metab* 93: 352–357, 2008
[2] Excludes one subject per group with missing Week 52 data (98.8% subjects completed study)
Top-line results from phase 3 heiGHt Trial.

TransCon hGH May "Rescue" Poor Responders to Genotropin

		IGF-1 SDS Ratio Change from Baseline (Poor Responders/Responders)	
		TransCon hGH / TransCon hGH	Genotropin / TransCon hGH
heIGHt TRIAL	Week 5	114%	52%
	Week 13	120%	54%
	Week 26	140%	46%
	Week 39	137%	56%
	Week 52	110%	57%
enliGHten TRIAL	Week 13*	103%	70%
	Week 26*	112%	84%

Genotropin Poor Responders have lower IGF-1 levels compared to responders

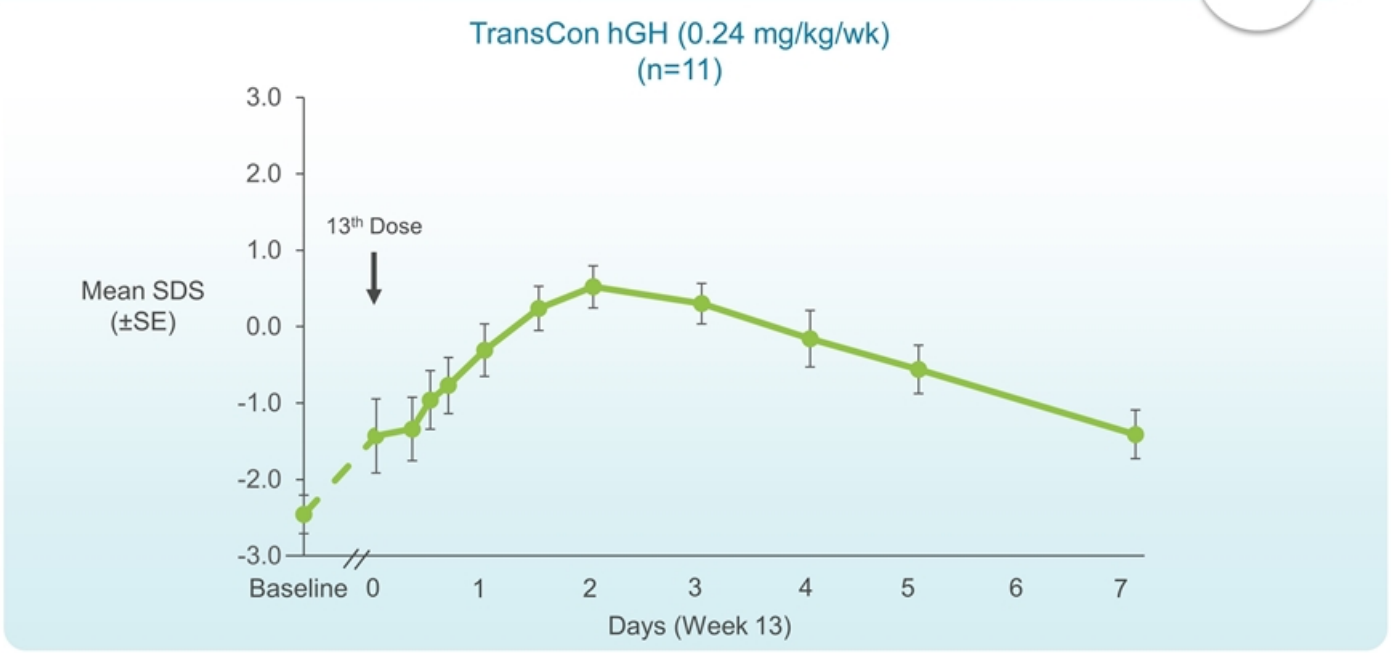
IGF-1 levels increased with TransCon hGH

Known variability in daily growth hormone absorption may explain variability in growth and IGF-1 response in poor responders[1]

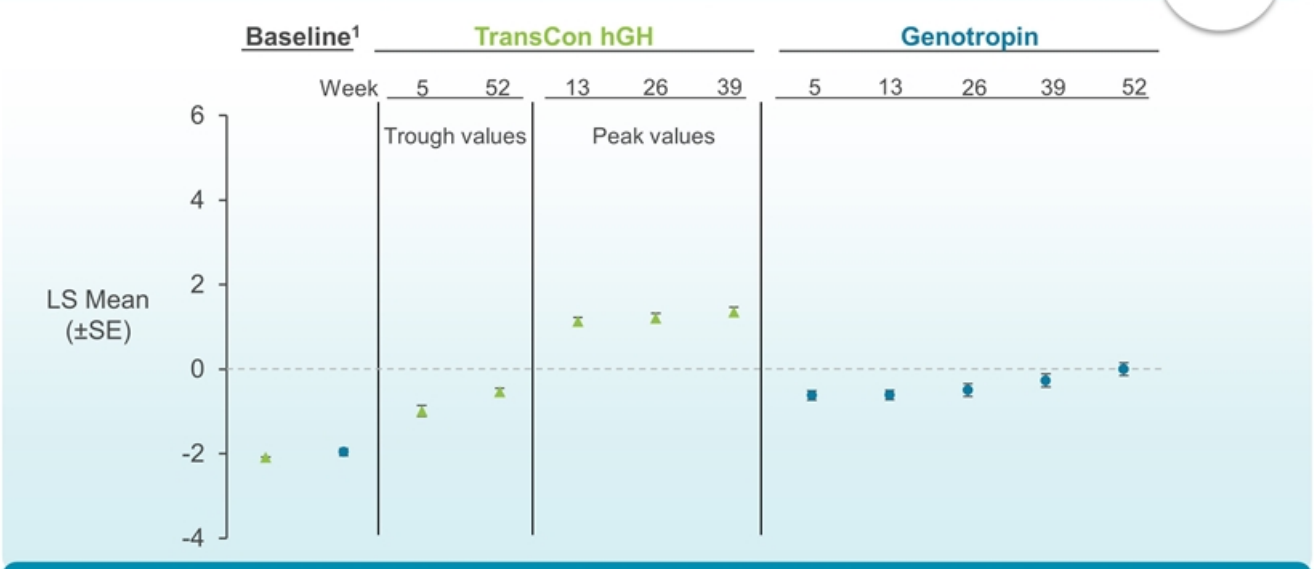
* Based on ongoing enliGHten Trial; Week 13 includes 77 subjects in TransCon hGH arm and 44 subjects in Genotropin arm; Week 26 includes 43 subjects in TransCon hGH arm and 21 subjects in Genotropin arm. Top-line results from phase 3 heiGHt Trial.

[1] GH&IGF Research 2018, 40: 61-68

IGF-1 Profile Over 1 Week



IGF-1 SDS Over 52 Weeks (N=161)



Estimated average IGF-1 SDS of 0.4 (average trough to peak) for TransCon hGH compared to an approximate average IGF-1 SDS of 0.0 for Genotropin consistent with the superior AHV

MMRM model.
[1] Baseline are observed mean values.
Top-line results from phase 3 heiGHt Trial.

IGF-1 Observations from heiGHt Trial

IGF-1 SDS	TransCon hGH (n=105) n (%)	Genotropin (n=56) n (%)
Maximum measurement >2.0 and ≤3.0		
At peak	20 (19.0)	NA
At trough	1 (1.0)	NA
Average (Genotropin)	NA	2 (3.6)
Maximum measurement >3.0		
At peak	14 (13.3)	NA
At trough	0	NA
Average (Genotropin)	NA	0
Consecutive measurements >2.0	9 (8.6)	1 (1.8)
Consecutive measurements >3.0	3 (2.9)	0
Annualized Height Velocity	11.2 cm/year	10.3 cm/year
Estimated Average IGF-1 SDS	0.4	0.0

NA = Not applicable
Top-line results from phase 3 heiGHt Trial.

IGF-1 Monitoring and Dose Adjustments in heiGHt

- IGF-1 SDS >2.0 at any visit should be confirmed by a second measurement if deemed clinically significant by the investigator
  - Samples should be collected 5-7 days post dose (TransCon hGH arm) or any day (Genotropin arm)
  - If the second IGF-1 SDS is also above 2.0 SDS, and of clinical concern, the dose may be decreased by ~20%

- 2/105 subjects on TransCon hGH reduced the dose due to high IGF-1 levels
- 1/56 subjects on Genotropin reduced the dose due to face/limb edema

Growth Hormone Research Society Position on LAGHs[1]

IGF1 measurements during LAGH administration

Unlike the experience with daily GH, both the appropriate timing of blood sampling and the interpretation of the IGF1 standard deviation score (SDS) in LAGH-treated patients are controversial. LAGH preparations differ in the kinetics of serum GH and IGF1 that they induce. Studies need to take into account the pharmacokinetics and pharmacodynamics of each product in order to gauge the optimal timing of IGF1 measurement. The goal is to maintain serum IGF1 concentrations within the normal age-appropriate range for a majority of the treatment period.

[1] European Journal of Endocrinology (2016) 174, C1–C8

Similar Change in Bone Age Over 52 Weeks

Bone Age	TransCon hGH (n=105) Mean Years	Genotropin (n=56) Mean Years
Baseline	5.84	5.98
Week 52	7.16	7.35
Change from Baseline	**1.36**	**1.35**

TransCon hGH demonstrated superior height velocity and advanced bone age at the same rate as Genotropin

Summary of Adverse Events: Safety Population

	TransCon hGH (n=105) n (%)	Genotropin (n=56) n (%)
Treatment-emergent Adverse Events (TEAEs)	81 (77.1)	39 (69.6)
TEAEs Related to Study Drug	12 (11.4)	10 (17.9)
Serious Adverse Events (AEs)	1 (1.0)	1 (1.8)
Serious AEs Related to Study Drug	0	0
TEAEs Leading to Any Action on Study Drug	2 (1.9)	1 (1.8)
TEAEs Leading to Discontinuation of Study Drug	0	0

- Adverse events for TransCon hGH consistent with type and frequency observed with Genotropin
- No serious adverse events related to study drug in either arm
- No treatment-emergent adverse event led to discontinuation of study drug in either arm

Adverse Events Reported by ≥5% of Subjects

Preferred Term	TransCon hGH (n=105) n (%)	Genotropin (n=56) n (%)
Pyrexia	16 (15.2)	5 (8.9)
Headache	13 (12.4)	7 (12.5)
Nasopharyngitis	12 (11.4)	8 (14.3)
Pharyngitis	10 (9.5)	10 (17.9)
Cough	10 (9.5)	4 (7.1)
Vomiting	9 (8.6)	3 (5.4)
Upper Respiratory Tract Infection	6 (5.7)	5 (8.9)
Respiratory Tract Infection	7 (6.7)	3 (5.4)
Secondary Hypothyroidism	7 (6.7)	3 (5.4)
Diarrhea	6 (5.7)	3 (5.4)
Pain in Extremity	4 (3.8)	4 (7.1)

No reports of adverse events of special interest (benign intracranial hypertension, scoliosis, slipped capital femoral epiphyses)

Stable Glycemic Parameters

TransCon hGH	Baseline	Week 5	Week 13	Week 26	Week 39	Week 52
HbA1c (%), mean	5.1	5.0	5.2	5.2	5.2	5.2

Genotropin	Baseline	Week 5	Week 13	Week 26	Week 39	Week 52
HbA1c (%), mean	5.0	5.0	5.1	5.1	5.1	5.1

Fasting glucose normal range 70 – 105 mg/dL

- Glycemic parameters were stable and within the normal range
- 2 subjects with high HbA1c (both 6.2%) at baseline remained stable throughout the trial

Low Incidence of Anti-hGH Binding Antibodies

Anti-hGH Binding Antibodies	TransCon hGH n=105 n (%)	Genotropin n=56 n (%)
Treatment-emergent positive	**7 (6.7)**	**2 (3.6)**
Transient, non-neutralizing	7 (6.7)	2 (3.6)
Persistent[1]	0	0
Neutralizing	0	0

[1] Persistent is defined as ≥16 weeks between the first and last positive post-baseline sample.
Top-line results from phase 3 heiGHt Trial.

heiGHt Trial Summary

- Treatment with TransCon hGH showed superiority over Genotropin in AHV at 52 weeks
  - Treatment difference in AHV reached statistical significance at Week 26 and onwards
  - Incidence of poor responders was ~3x lower in the TransCon hGH arm compared to the Genotropin arm
  - Only 2 dropouts; one in each treatment arm
- Safety profile of TransCon hGH was consistent with daily Genotropin
  - Low Incidence of anti-hGH binding antibodies and no neutralizing antibodies
  - Similar local injection site tolerability between treatment arms
- IGF-1 SDS scores were generally within the normal range following treatment for both groups
- BMI was statistically unchanged in both arms and trended toward normalization
- TransCon hGH advanced bone age at the same rate as Genotropin

Phase 3 fliGHt Trial Design

146 children with GHD (143 treatment-experienced)

Key Inclusion Criteria

- Investigator-determined GHD with supporting biochemical and auxologic criteria
- Age 6 months – 17 years old
  - Tanner stage <5
  - Open epiphyses
  - Treated with commercially-available daily hGH therapy ≥0.20 mg/kg/week for 13 – 130 weeks
  - Children <3 years could have been treatment-naïve

Key Endpoints

- Adverse events
- Injection site reactions
- Incidence of anti-hGH antibodies
- Annualized height velocity at 26 weeks
- Change in height SDS at 26 weeks
- Proportion of subjects with IGF-1 SDS in the normal range (0.0 to +2.0) at 26 weeks
- PK/PD in subjects <3 years
- Preference and satisfaction with TransCon hGH

fliGHt Baseline Demographics

	TransCon hGH (N=146) Mean
Male (%)	75.3
Age (years)	10.6
Age Range (years)	1 - 17
Height SDS	-1.42
BMI (kg/m^2)	17.5
Δ Average Parental Height SDS	-1.14
IGF-1 SDS	0.9
IGF-1 SDS Range	-1.9 – 4.0
Caucasian (%)	84.9
Recruited in North America (%)	95.2

Disease Characteristics at GHD Diagnosis

	n	TransCon hGH (N=146) Mean
Height SDS	138	-2.1
Peak Stimulated GH (ng/mL)	143	5.9
IGF-1 SDS	60	-1.27
Chronologic Age (years)	120	9.42
Bone Age (years)	120	8.23
Delay in Bone Age (years)	120	1.19

Previous Daily hGH Use

	TransCon hGH (N=146)
Daily hGH Dose Prior to Trial (mg/kg/week), mean (range)	0.29 (0.13 – 0.49)
Treatment-Experienced, n (%)	143 (97.9%)
<6 Months	40 (27.4%)
≥6 to <12 Months	32 (21.9%)
≥12 to <18 Months	28 (19.2%)
≥18 Months	43 (29.5%)
Treatment-Naïve, n (%)	3 (2.1%)

Summary of Adverse Events

	TransCon hGH (N=146) n (%)
Treatment-emergent Adverse Events (TEAEs)	83 (56.8)
TEAEs Related to Study Drug	6 (4.1)
Serious Adverse Events (AEs)	1 (0.7)*
Serious AEs Related to Study Drug	0
TEAEs Leading to Discontinuation of Study Drug	0

* One subject reported two serious AEs; both considered unrelated

Stable HbA1c During Trial

	Baseline N=146	Week 13 n=142	Week 26 n=143
HbA1c (%), mean	5.2	5.2	5.2

IGF-1 SDS Observations from fliGHt Trial

IGF-1 SDS	Baseline On daily GH n=145	Week 13 Post-dose Day 5 (±1 day) n=143	Week 26 Post-dose Day 5 (±1 day) n=141
Mean (SD)	0.9 (1.3)	1.6 (1.2)	1.7 (1.2)
Categories			
IGF-1 SDS >2 and ≤3, n (%)	27 (18.6)	38 (26.6)	33 (23.4)
IGF-1 SDS >3, n (%)	5 (3.4)	17 (11.9)	22 (15.6)

No IGF-1 measurements were reported as adverse events

Post-dose Day 5 estimates average IGF-1 levels over the week
Top-line results from phase 3 fliGHt Trial.

Mean AHV at Week 26 by Subgroups

	AHV at Week 26 (cm/year)
	TransCon hGH (N=146) Arithmetic Mean
Age	
<3 years	16.2
≥3 and <6 years	10.0
≥6 and <11 for girls; ≥6 and <12 for boys	8.2
≥11 for girls; ≥12 for boys	9.0
Gender	
Male	9.0
Female	9.1
Peak Stimulated GH	
≤5 ng/mL	9.6
>5 ng/mL	8.6

fliGHt Trial Summary

- Treatment with TransCon hGH in the fliGHt trial was generally safe and well-tolerated
  - Only 2 dropouts
- No serious adverse events related to study drug and no treatment-emergent adverse events leading to discontinuation of study drug
  - Safety profile consistent with heiGHt Trial
  - Stable HbA1c, morning cortisol and free thyroxine levels
  - For children <3 years, no unexpected safety issues observed
  - Well-tolerated injections
- IGF-1 SDS were generally within the normal range and no IGF-1 elevations were reported as adverse events
- Annualized height velocity was as expected in the context of subject characteristics
  - For children <3 years, AHV of 16 cm/year observed

Auto-Injector Designed to Improve Adherence

Key Features

- Simple operation with few user steps
- Single low-volume (<0.60mL) injection for patients ≤60kg
- Small needle, comparable to daily hGH (31G, 4mm)
- Room temperature storage
- No waste due to empty-all design
- Bluetooth® connectivity enabled for automatic data capture
- Device lifespan at least 4 years

Auto-Injector introduced into the enliGHten Trial and available at commercial launch

TransCon hGH Phase 3 Program

heiGHt TRIAL N=161

- Treatment-naïve subjects
- Top-line data reported

fliGHt TRIAL N=146

- Subjects previously treated (n=143) and treatment-naïve (<3 years, n=3)
- Top-line data reported

98% of eligible subjects from heiGHt and fliGHt rolled over to enliGHten

enliGHten TRIAL

Extension trial (N=~300)

Regulatory filings (BLA H1 2020, MAA H2 2020)

TransCon hGH: Highlights

- Two phase 3 trials heiGHt TRIAL and fliGHt TRIAL demonstrated potential of TransCon hGH:
  - Superior efficacy in a treatment-naïve population in heiGHt Trial
  - Fewer poor responders compared to daily hGH
  - Comparable safety, tolerability and immunogenicity to a daily hGH for both treatment-naïve and treatment-experienced populations
- Auto-Injector introduced into enlIGHten TRIAL
- Safety, tolerability and efficacy consistent between phase 2, heiGHt and fliGHt Trials
- BLA filing planned H1 2020 and MAA in H2 2020

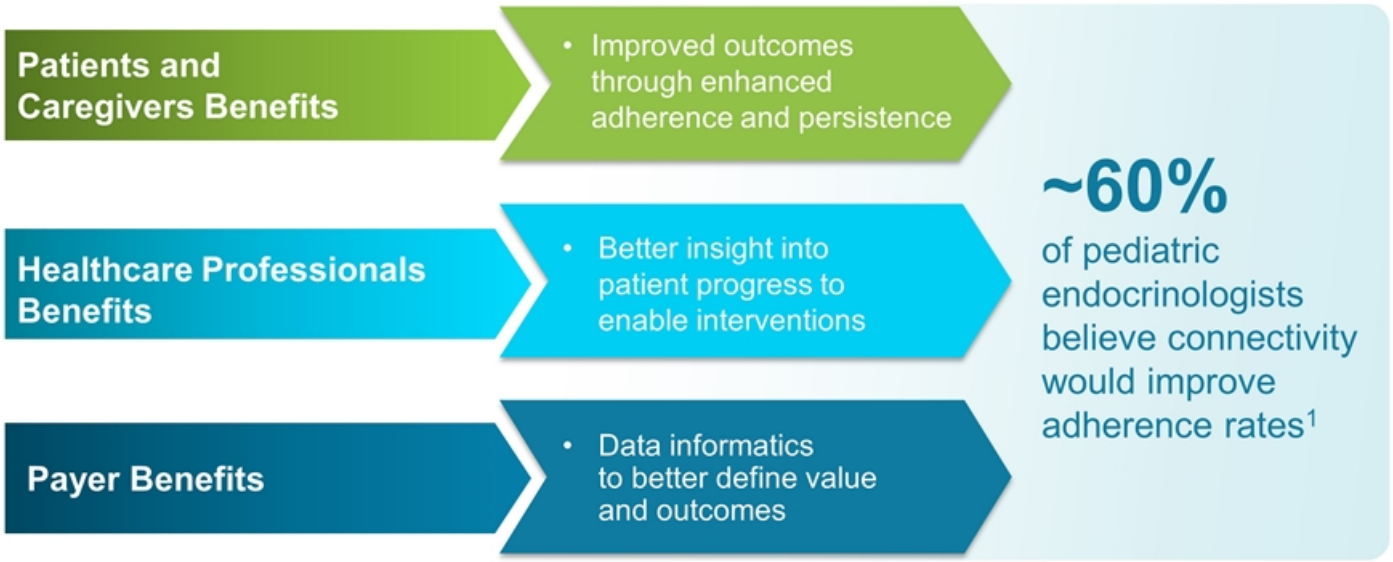
Connected Healthcare Platform

Thomas Ørts Pedersen, Ph.D.
Director, Product Development, CMC Pharmaceutical & Device Development

Ascendis Pharma Connected Healthcare (CH) Vision

Become a Leader in Innovative Patient Care Solutions that Integrates Data Informatics to Enhance Patient Care at the Individual and Population Levels

Connected Healthcare Value Proposition



[1] Data on file from 100 endocrinologist interviews conducted by Ascendis Pharma in 2018.

Connectivity Platform: Targets for Endocrinology Products

TransCon hGH

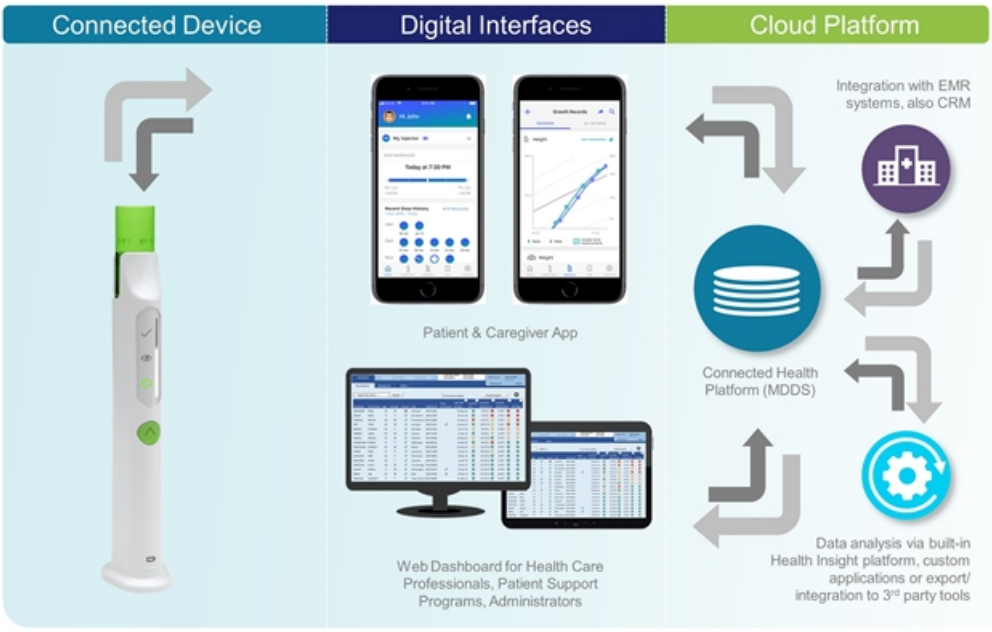
- Suite of patient and caregiver app, HCP and patient support program (PSP) web dashboard and backend/cloud solution with analytics capabilities
- Manual dose recording solution ready for potential launch
- Automated Bluetooth® dose recording solution ready for planned supplemental BLA

TransCon PTH

- Suite of patient and caregiver app, HCP and PSP web dashboard and backend/cloud solution with analytics capabilities (leverage the hGH suite/setup)
- Development of automated, Bluetooth dose recording solution

ascendis pharma

TransCon hGH: Attributes of the Planned CH Infrastructure



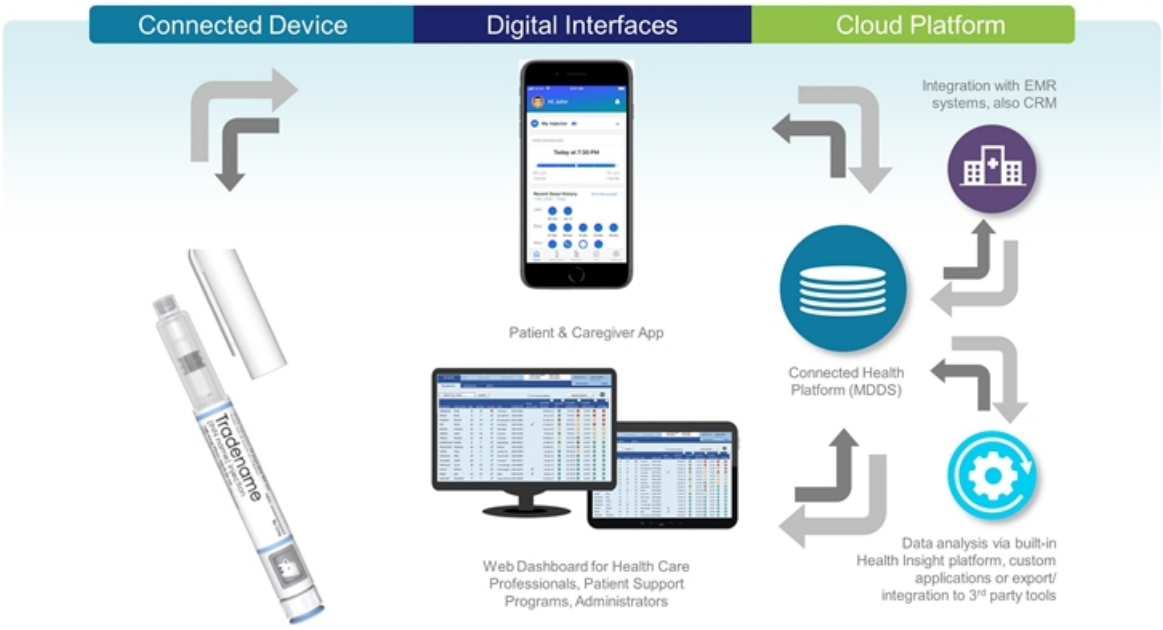
- System records date, time and dose
- Opportunity for digital patient interaction, including patient use app, ongoing reminders and feedback
- Integration with physician, provider via HCP dashboard and data analytics

Technical Overview: Planned TransCon hGH Systems

	Initial Launch	Supplemental BLA
 **Auto-Injector (AI)**	• Introduce easy-to-use AI • Experience from phase 3 enliGHten Trial	• Introduce Bluetooth connectivity and automated dose recording solution
 **CH App[#] /Dashboard[+]/ Cloud**	• Designed for manual data entry via app • App and dashboard connected to CH platform	• Designed for connectivity • App and dashboard connected to CH platform

[#]: For IOS/Android; [+]: web based

TransCon PTH: Leverages hGH Connectivity Infrastructure



Connected Healthcare to Benefit Patient Experience

- Proprietary Auto-Injector designed to improve patient experience and outcomes
- Introduced into enliGHten Trial in June 2019
  - Provides sufficient patient data to support AI as part of initial BLA submission
- Development of a CH suite underway in accordance with Ascendis Pharma's vision of creating potential best-in-class products

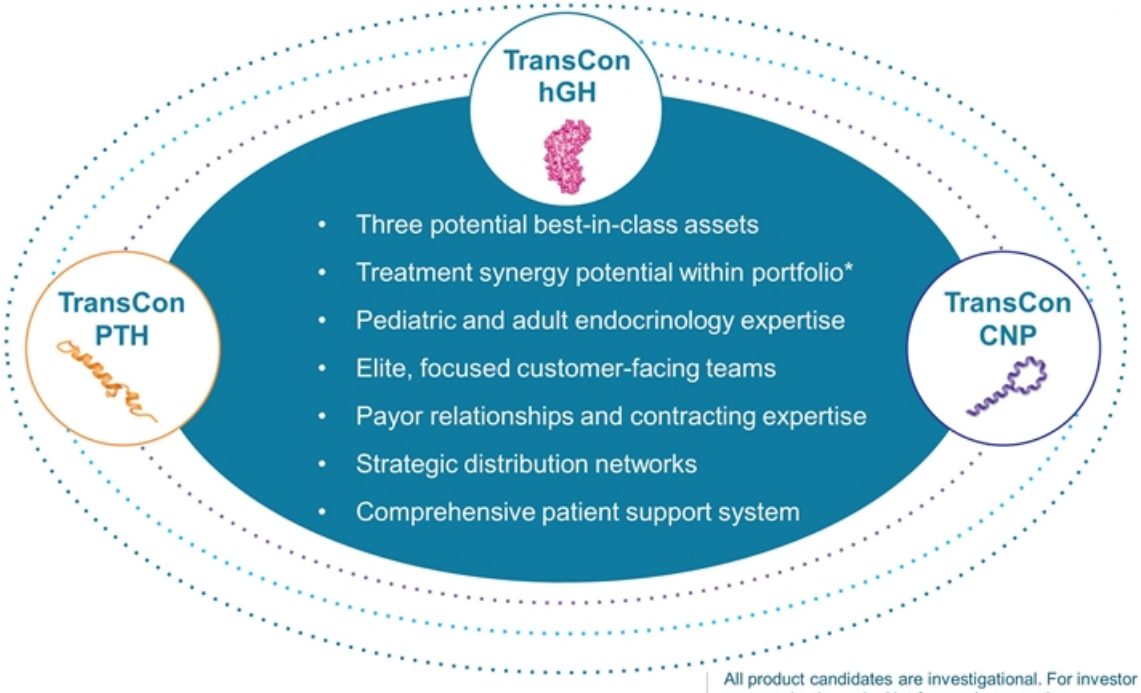
Commercialization Update

Tom Larson
SVP, Chief Commercial Officer

Commercial Vision

To Create a Market Leading Brand in Every Product Category and to become a Trusted, Respected Partner within Every Customer Segment

Robust Endocrinology Rare Disease Pipeline with Product and Treatment Synergies



*Planned

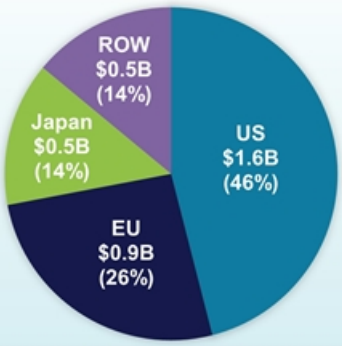
All product candidates are investigational. For investor communication only. Not for use in promotion.

ascendis pharma

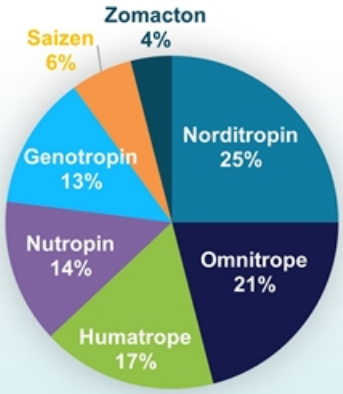
The Growth Hormone Market: Ripe for Disruption

- Large, established global market of ~$3.5 billion and growing (2.4% CAGR)[1]
- Concentrated prescriber audience
- Fragmented existing market with the same undifferentiated daily hGH molecule
- Limited innovation since rhGH was introduced >30 years ago

Worldwide Market (Value) by Region[1]



US Market Share (Value) by Brand[2]

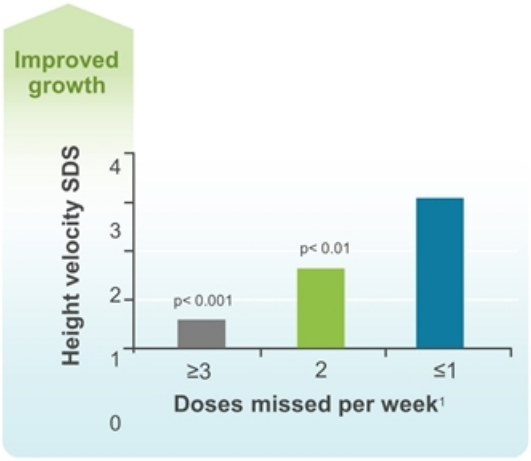


[1] Ascendis Pharma market assessment 2015.
[2] Data on file from 100 endocrinologist interviews conducted by Ascendis Pharma in 2018.

Daily Growth Hormone: The Problem!

In the 1st year, two of three patients miss >1 injection on average per week[1]

Impact of poor adherence

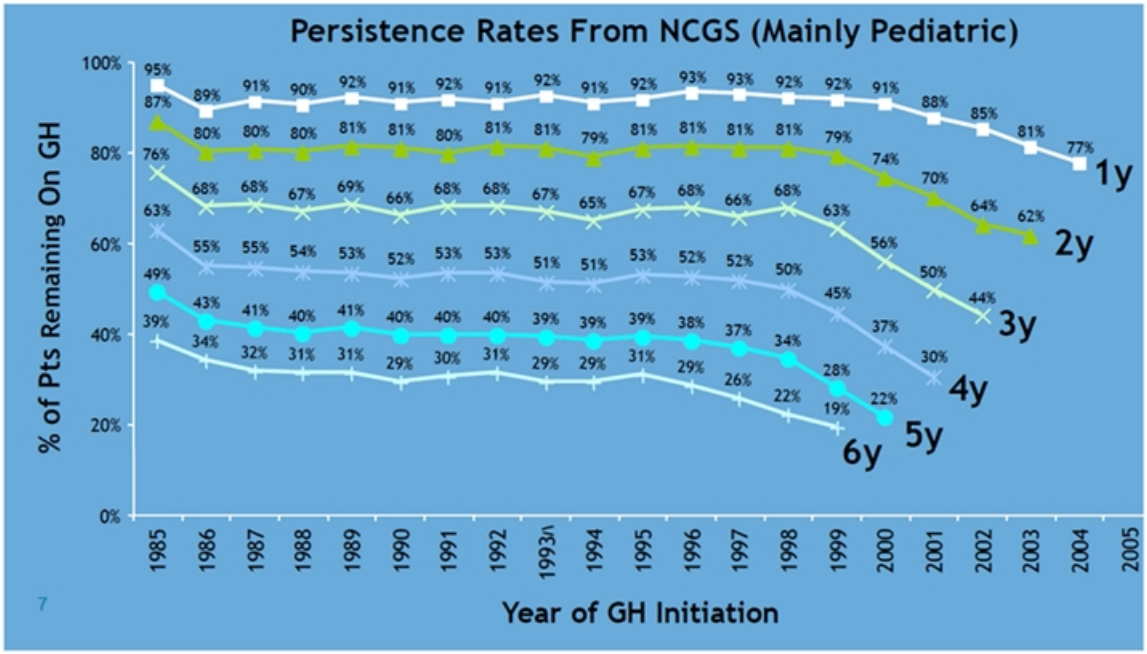


Drivers of poor adherence…outcome

- Patient: Burden of injection is significant[2]
- Parent: Experience significant stress and guilt injecting their child[2]
- Children prefer weekly to daily dosing[3]
- Bioavailability of daily GH varies up to 44%[4]

[1].PLoS ONE 2011, 6(1):e16223 [2] Qual Life Res 26:1673–1686 [3] Value in Health, Vol. 21, S139–S140
[4]Growth Horm IGF Res 40:61-68

Persistence Rates Among Nutropin Patients Decline Over Recommended Treatment Period



Rosenfeld R, Bakker B. Compliance and persistence in the growth hormone treated population (abstract). Presented at ENDO 2014

TransCon hGH: Commercialization Strategic Imperatives

Strategic Imperative #1: Drive Rapid Market Penetration

KEY CUSTOMER SEGMENTS

Mobilize Patient-Caregiver

- Drive broad education and awareness
- Create urgency to switch

Educate Pediatric Endocrinologists and Ped Endo Nurses

- TransCon hGH: The *"New Standard"* for naïve and existing patients
- Differentiate benefits of TransCon…the only unmodified LAGH in clinical development
- Initiatives to drive rapid patient adoption

Mitigate Barriers with Payers

- Drive patient demand
- Innovative market access "value" strategy
- Build long-term partnership in endocrine health

ascendis pharma

Strategic Imperative #2: Expand the Market

TransCon hGH Benefits Realized

- Enhanced patient adherence and persistence
- Expand in patients unwilling to take daily injections
- Rescue failed patients

Connected Healthcare Platform

- Enhance patient engagement, education, adherence and persistence

Leverage Pipeline

- Innovative life-cycle-management and potential new treatment paradigms
- Potential new fixed dose combination therapies

ascendis pharma

Strategic Imperative #3: Ensure Sustainable Success

Leverage Pipeline and TransCon Platform

- Robust clinical development plan (life-cycle management)
- Potential best-in-class value proposition (more indications)
- To drive preferential payer formulary status

ascendis pharma

Clinical Evidence Expected to Pave Way for Rapid Adoption*

heiGHt TRIAL

Unparalleled clinical evidence provides compelling value proposition and clear pathway for starting **Tx-naïve** patients

fliGHt TRIAL

Confidence in **switching** patients for rapid market penetration

enlIGHten TRIAL

Provides assurance with **long-term** safety and efficacy assessments

*Based on results from the heiGHt and fliGHt trials. TransCon is not approved by FDA or EMA.

ascendis pharma

TransCon hGH Expected to Deliver on Patient Unmet Need

Product X (TransCon hGH) Clinical Value
Average rating on a scale of 1 to 9
[based on non-inferior efficacy]

TransCon hGH Expected to Deliver on Patient Unmet Need[1]

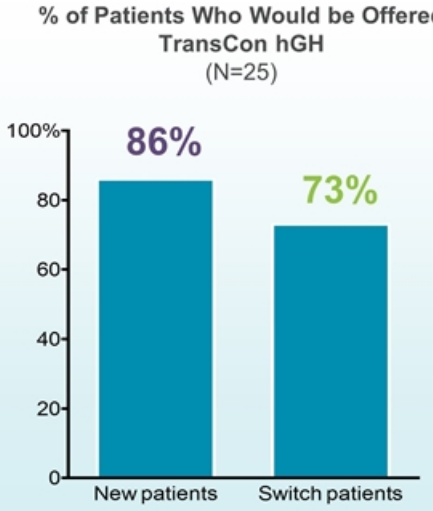
Product X (TransCon hGH) Clinical Value
Average rating on a scale of 1 to 9
[based on non-inferior efficacy]

> ***I don't know why you would use a daily when you have this***
>
> *Pediatric Endocrinologist*

[1] Data on file from 25 physician and 20 patient/caregiver interviews conducted and analyzed by Ascendis Pharma in 2018. *7.5 or > considered "outstanding"*

With Non-inferior Efficacy, Physicians Would Offer TransCon hGH to Most Eligible Patients[1]

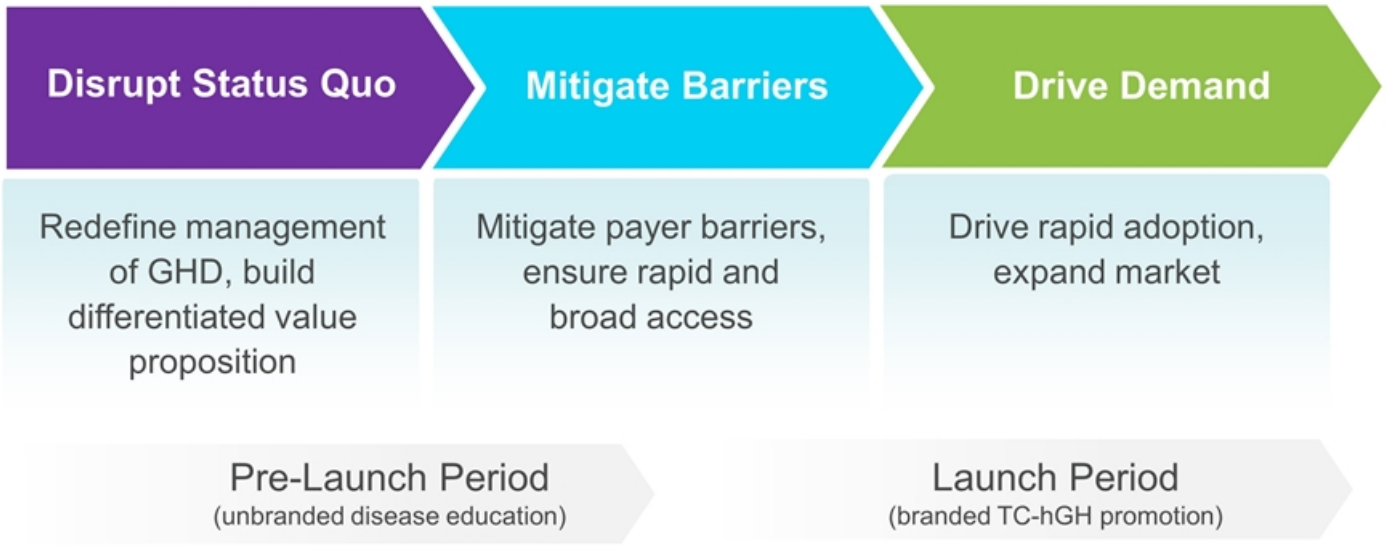
100% of Patients with PGHD Considered Eligible for TransCon hGH



> ***This is terrific…No antibodies, small needle, variety of cartridge and dosing is all great***
>
> *Pediatric Endocrinologist*

[1] Data on file. Analyzed by Ascendis Pharma. Qualitative market research with N=25 Physicians in 2018.

Planned Go to Market Strategy



Why Use TransCon hGH?

- Expected Value Proposition
  - Weekly administration
  - The only LAGH in clinical development which releases unmodified hGH to adequately address the totality of the disease
  - Superior efficacy compared to daily hGH (heiGHt)
  - Fewer poor responders than daily hGH
  - Compelling clinical evidence for both treatment-naïve and switch patients
  - Comparable safety and tolerability to daily hGH
  - Fully integrated connected health care platform
  - Easy-to-use Auto-Injector
    - Room temperature stability
    - Small 31-gauge, 4 mm needle
    - Small volume (0.6 ml)

Why Not?

TransCon hGH

Summary and Q&A

Global Clinical Reach

Region	US	EU	Japan	South Korea	China
Nonclinical packet acceptable for regulatory filing	✓	✓	✓	✓	✓
Regulatory concurrence with proposed clinical development plan	✓	✓	Planned phase 3 initiation 2020* (40 subjects)	✓	Planned phase 3 initiation 2019** (75 subjects)

* Ethnobridging is required before initiation of Phase 3
** Phase 3 being conducted by Visen Pharma

TransCon hGH: Raising the Bar

- Phase 3 heiGHt Trial demonstrated superior efficacy of TransCon hGH in pediatric GHD, with comparable safety and tolerability
- BLA filing expected H1 2020 and MAA filing expected H2 2020
- Global clinical reach aligned with regional regulatory agencies; phase 3 planned to be initiated in China 2019 and in Japan 2020
- Multiple label expansions planned: Adult GHD program to be initiated 2020
- Easy-to-use Auto-Injector with automatic data capture and integration with connected healthcare platform aims to improve adherence
- Commercial-scale manufacturing and supply chain established
- Commercialization leadership team, infrastructure and launch plan in place
- 17 independent patent filings, including composition-of-matter and device covering TransCon hGH, provide potential protection into 2039

Q&A

Today's Agenda

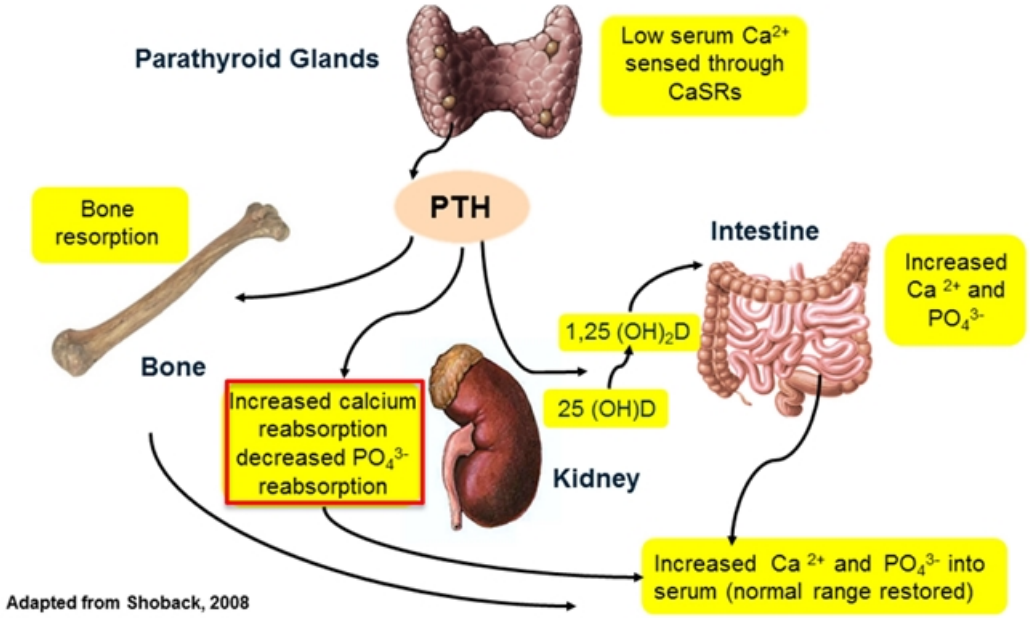
9:00-9:05 a.m.	Welcome & Agenda Overview Scott T. Smith
9:05-9:15 a.m.	Vision 3x3 Jan Møller Mikkelsen
9:15-9:30 a.m.	TransCon Platform & Product Innovation Kennett Sprogøe, Ph.D.
9:30-10:05 a.m.	TransCon hGH Jonathan Leff, M.D.
10:05-10:15 a.m.	Connected Healthcare Platform Thomas Ørts Pedersen
10:15-10:30 a.m.	Commercialization Update Tom Larson
10:30-10:40 a.m.	Q&A: TransCon hGH
10:40-10:50 a.m.	Break
10:50-11:20 a.m.	**TransCon PTH** David Karpf, M.D. & Nyssa Liebermann Noyola
11:20-11:35 a.m.	**TransCon CNP** Kennett Sprogøe, Ph.D.
11:35-11:45 a.m.	**Q&A: TransCon PTH & TransCon CNP**
11:45-12:05 p.m.	**Introducing Oncology** Jan Møller Mikkelsen & Juha Punnonen, M.D., Ph.D.
12:05-12:20 p.m.	**IO & IT Treatments: Challenges & Promise** Ezra Cohen, M.D.
12:20-12:40 p.m.	**Oncology Product Candidates** Juha Punnonen, M.D., Ph.D.
12:40-12:50 p.m.	**Q&A: Oncology**
12:50-1:00 p.m.	**General Q&A & Closing Remarks** Jan Møller Mikkelsen

ascendis pharma

TransCon PTH: PTH Replacement Therapy for Hypoparathyroidism

David B. Karpf, M.D.
VP, Clinical Development

PTH Controls Serum Calcium, Serum Phosphate, Urinary Calcium and Bone Turnover



Adapted from Shoback, 2008

Hypoparathyroidism: Severe Short-term Complications

Debilitating Symptoms

Hypocalcemia
Paresthesias, muscle cramps, tetany, laryngospasm, seizures, coma

Brain fog

Anxiety due to "fear of crash"

Hypercalcemia
Nocturia, polyuria, constipation, muscle weakness, coma

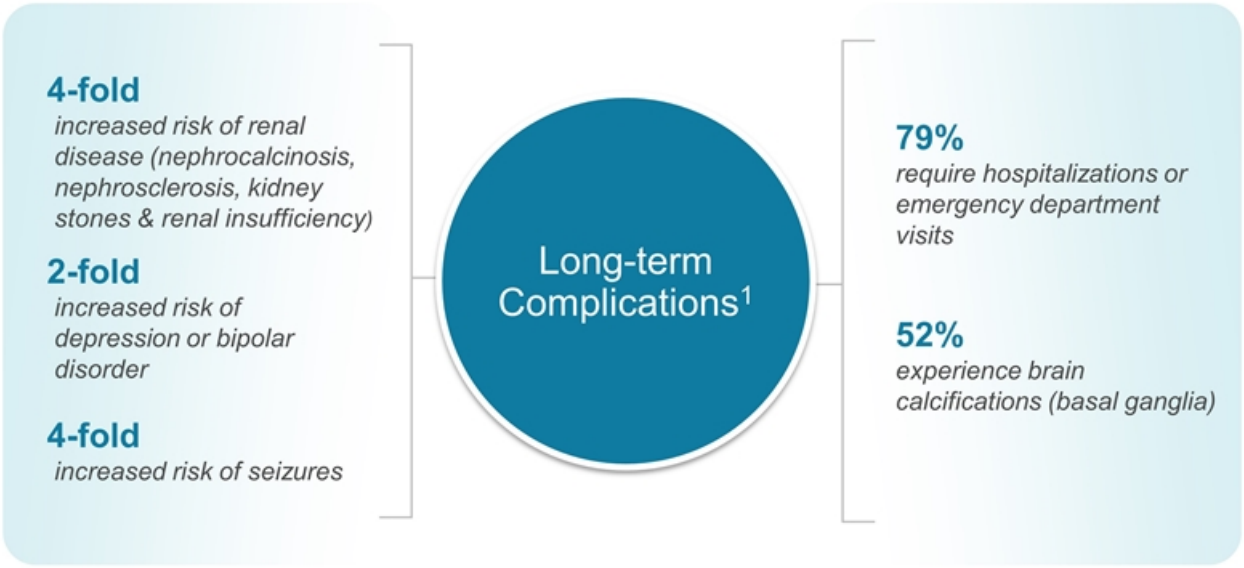
Reduced QOL

85%
Report inability to perform household activities[1]

76%
Either unable to work or report significant interference with work d/t HP symptoms[2]

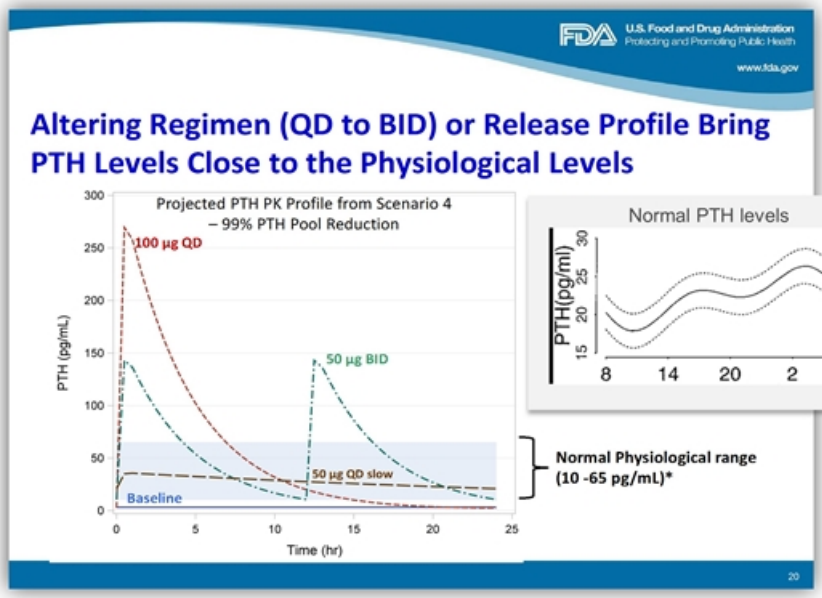
[1] Endo Pract. 2017, 20(7):671-679
[2] 2019 Ascendis Pharma HP Patient Experience Research

Hypoparathyroidism: Severe Long-term Complications



[1] J Bone Miner Res 2013, 28: 2570-2576; J Clin Endocrinol Metab 2012, 97(12): 4507-4514; J Bone Miner Res 2013, 28: 2277-2285

Constant Normal Level of PTH is Optimal - FDA Perspective[1,2]

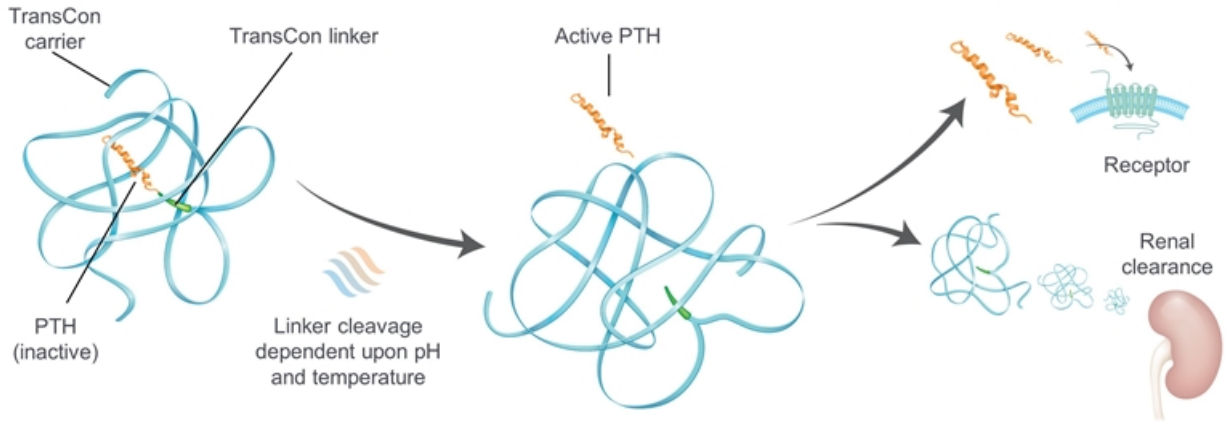


- Daily PTH(1-84) increases serum calcium for ~20 hours
- Control of urinary calcium excretion is short-lived (10-12 hours); renal reabsorption of calcium follows PK profile[1,2]
- Regulatory view based on NIH studies demonstrated continuous SC infusion of PTH(1-34) superior in patients with HP vs BID injections, normalizing sCa, sP, uCa, and bone turnover despite a >60% lower daily dose[3,4]

[1,2] FDA presentation: Natpara Advisory Committee, September 12, 2014; Clin Pharmacol Ther. 2019 105(3):710
[3,4] J Clin Endo Metab 2012 97(2);391–399; J Pediatr 2014 165(3);556-563

ascendis pharma

TransCon PTH Design

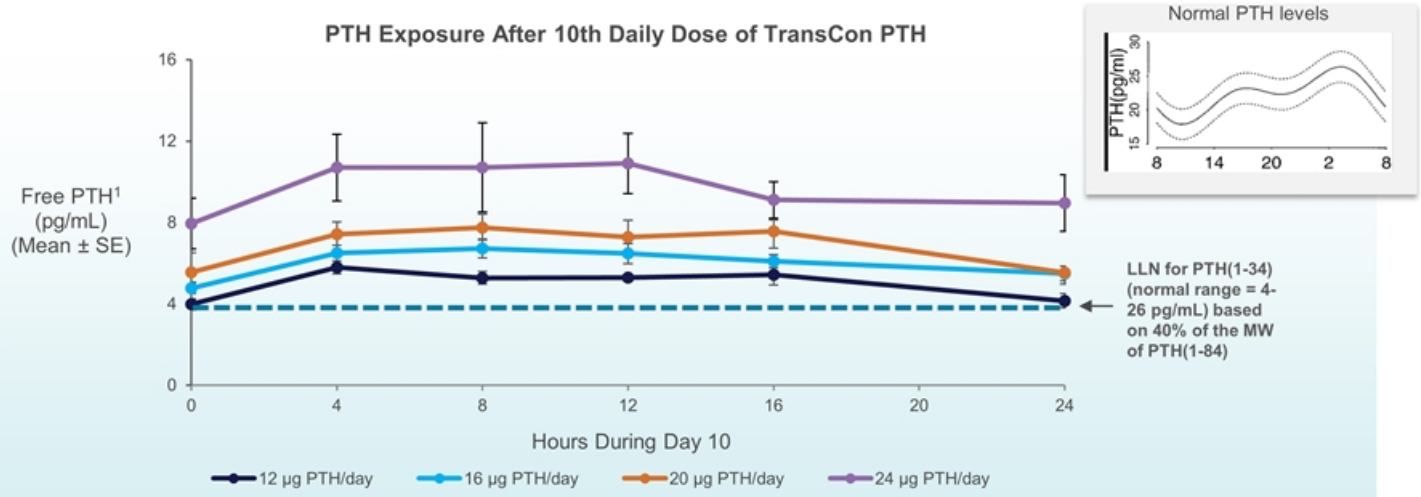


- TransCon PTH is a sustained-release prodrug designed to provide stable PTH levels in the physiological range for 24 hours/day
- TransCon PTH designed to normalize blood and urinary calcium levels, serum phosphate and bone turnover

Phase 1 Trial Designed to Evaluate PK/PD

- 132 normal healthy subjects (male and female)
- Cohorts of 10 subjects (8 active, 2 placebo)
- 7 single-ascending dose (SAD) cohorts (3.5 to 124 µg)
- 6 multiple-ascending dose (MAD) cohorts (3.5 to 24 µg/day)
- Key endpoints:
  - PK: Free PTH
  - PD: Adjusted serum calcium and phosphate, FECa, intact PTH(1-84), bone turnover markers

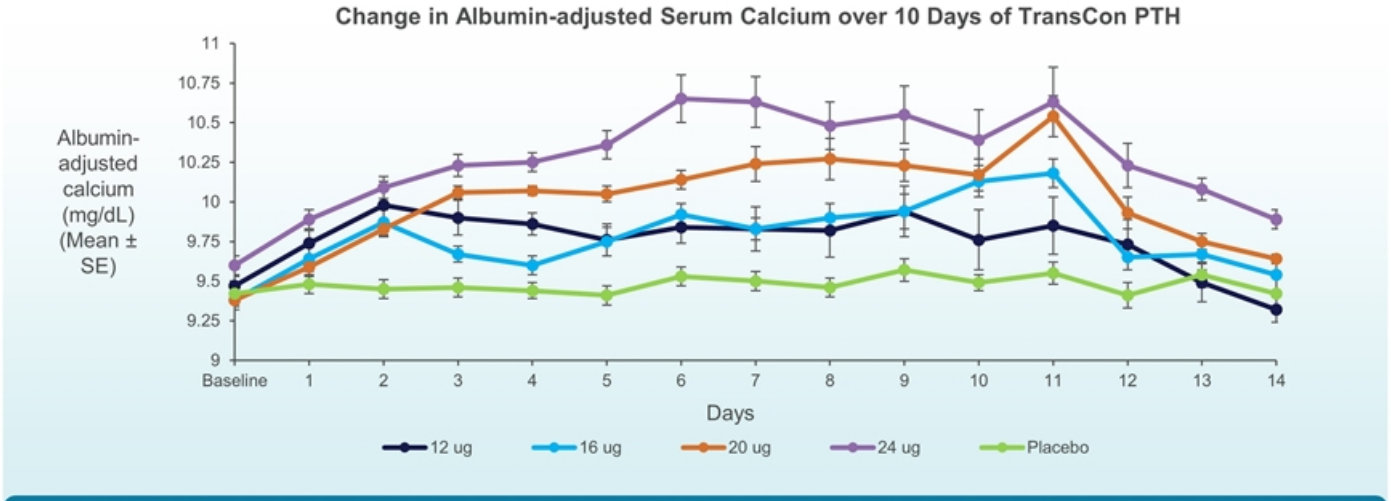
Phase 1: PK Data Support Infusion-like Profile over 24 Hours



- TransCon PTH daily dosing for 10 days provided a flat infusion-like profile with low PTH peak-to-trough ratio at day 10
- Dosing in evening predicted to recapitulate the diurnal exposure of endogenous PTH in normal subjects

[1] PTH measured as Free PTH(1-34) and Free PTH(1-33)
Analyses from TransCon PTH Phase 1 trial; data not shown for doses <12 µg/day, as levels of Free PTH are BLQ.
Poster presented at ECTS 2019

Dose-Dependent Increase of Serum Calcium

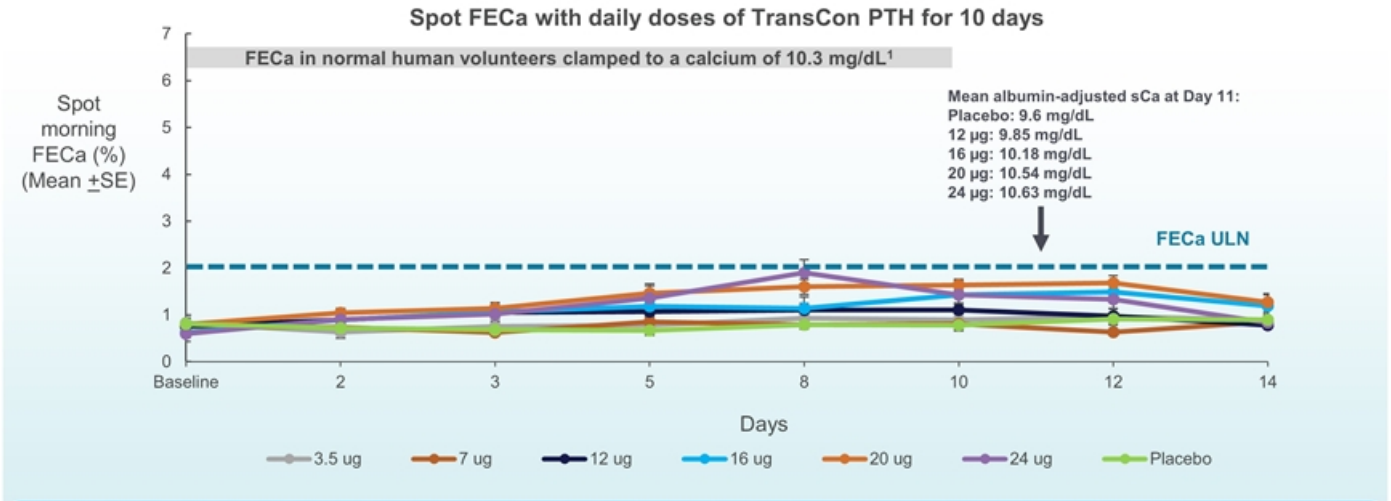


TransCon PTH daily dosing for 10 days provided dose-dependent increase of serum calcium, with more stable calcium levels over the day

Analyses from TransCon PTH Phase 1 trial; doses <12 µg/day not shown as no significant increase in calcium at these doses.
Poster presented at ECTS 2019

ascendis pharma

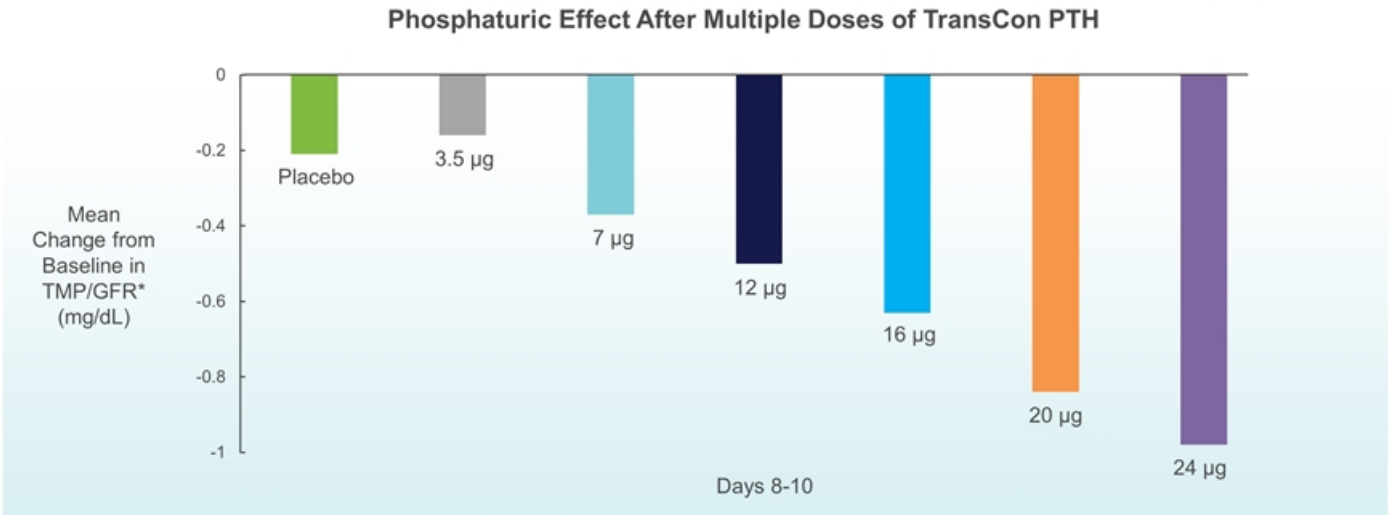
Control of Urinary Calcium Despite Mild Hypercalcemia with Multiple Doses



Despite sCa at as high as 11.2 mg/dL (with increased renal filtered Ca), FECa (renal calcium excretion) remained normal; well below values reported for NHVs clamped to serum Ca of 10.3 mg/dL[1], reflecting potent PTH-mediated renal Ca reabsorption

[1] J Clin Endocrinol Metab 2001, 86(4): 1525-1531
Poster presented at ECTS 2019

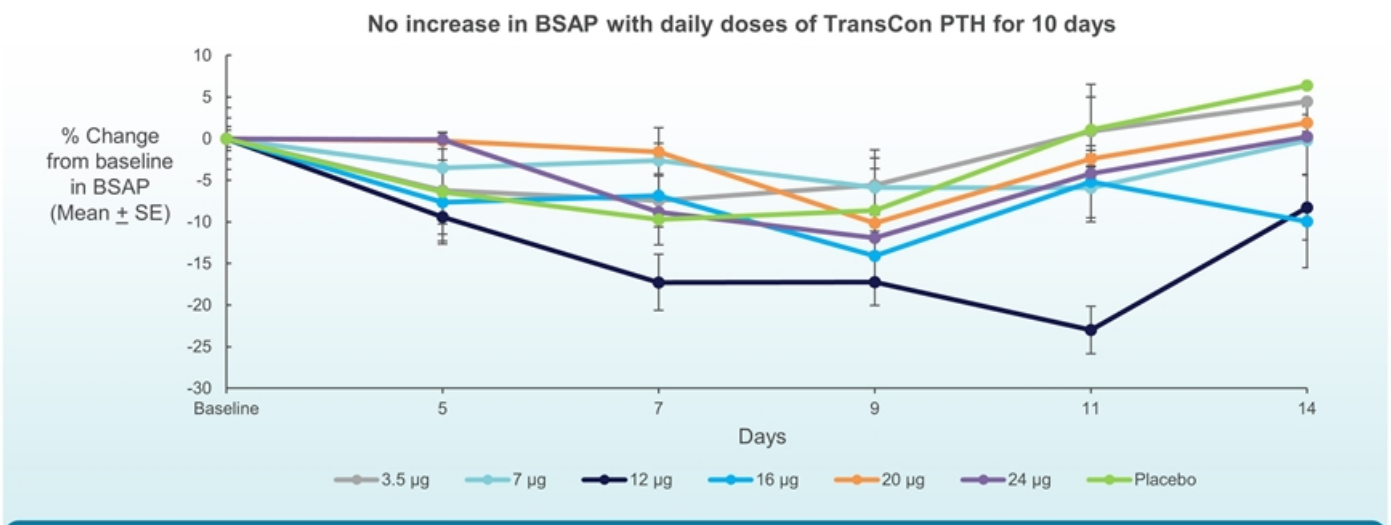
Dose-Dependent Phosphaturic Effect



TMP/GFR (phosphate excretion in urine) showed significant dose-dependent reduction (p=0.0022 for linear dose response) resulting in significant reduction in sP (p=0.0430)

* TMP = Tubular maximum absorption of phosphate; GFR = Glomerular filtration rate

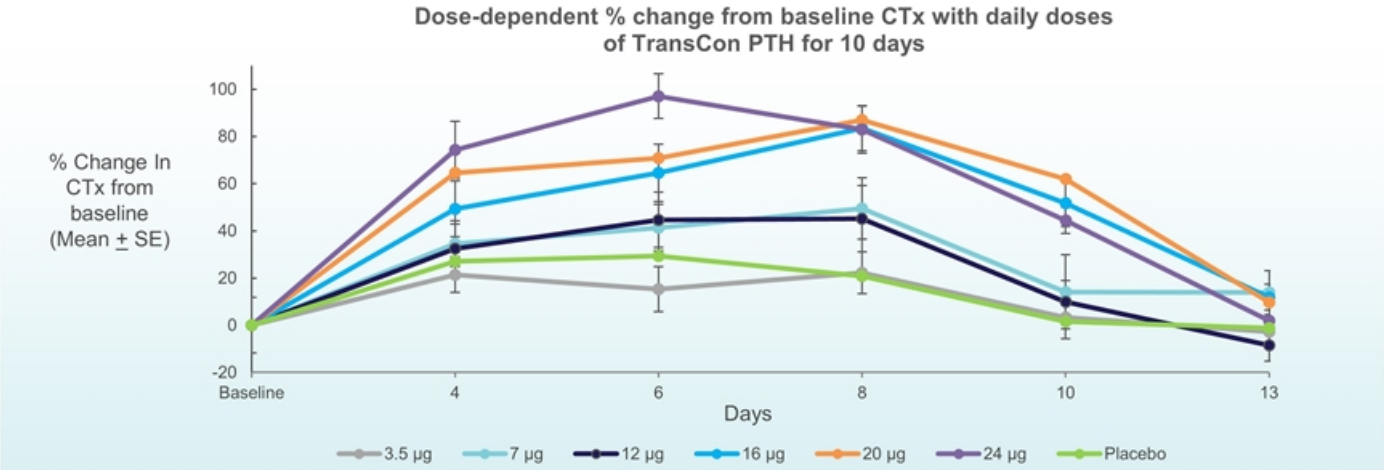
No Increase in BSAP: No Evidence of Anabolic Effect



At baseline, BSAP (bone-specific alkaline phosphatase) was similar among treatment groups and remained stable over 10 days of dosing, suggesting TransCon PTH has no anabolic effect

ascendis pharma

Modest and Only Transient Increase in Serum CTx



- CTx showed a transient modest increase after repeat daily doses of ≥16 µg/day, less than the sustained increase (100-200%) with daily PTH(1-84) and PTH(1-34)
- No increase was seen in urine NTx (data not shown)

Phase 1 Trial Safety Summary

- Generally well-tolerated
- 2 placebo subjects (vs. 0 active subjects) discontinued due to SAEs
- 4 subjects experienced SAEs, all of which were unrelated to study drug or placebo
  - SAD: 1 placebo subject (“bacteremia”) (withdrew)

    1 active (12 µg) subject (“catheter site phlebitis”)
  - MAD: 1 placebo subject (“catheter site phlebitis”) (withdrew)

    1 active (12 µg/day) subject (“post-viral neutropenia”)
- No PTH antibodies were seen
- Dose-limiting toxicity (DLT) was not reached in the highest SAD cohort (124 µg)
- DLT (vasodilatory AEs) was reached in the highest MAD cohort (24 µg/day), in 4/8 (50%) active vs 2/2 (100%) placebo subjects

TransCon PTH: Phase 1 Summary

- Half life of ~60 hours
- Flat, infusion-like profile within the physiological normal concentration range with daily administration
- Dose-dependent increase in serum calcium, decrease in serum phosphate, and suppression of endogenous PTH(1-84)
- Maintained normal urine calcium excretion despite mild hypercalcemia
- Well-tolerated, with no drug-related serious or severe adverse events

TransCon PTH: Target Profile

A sustained-release PTH that produces 24-hour PTH levels within the normal range, similar to continuous pump delivery

- Remove current standard of care (active vitamin D and calcium)
- Control hypo- and hypercalcemic episodes
- Control hypercalciuria
- Control hyperphosphatemia
- Normalize bone turnover, leading to a modest decrease (to normal) in trabecular bone mass, and no significant decline in cortical bone mass
- Absence of an anabolic effect may predict a lower or absent theoretical osteosarcoma risk

TransCon PTH Phase 2 Trial Design

PaTHforward TRIAL

~40 adult subjects with HP currently receiving standard of care (active vitamin D + calcium)

Primary Composite Endpoint (4 weeks)

Proportion of subjects with:

- Normal serum calcium; **AND**
- Normal FeCa (or at least 50% decrease from baseline); **AND**
- Off active vitamin D; **AND**
- Taking ≤1,000 mg/day calcium

Key Secondary Endpoints (4 weeks)

- Primary composite **AND** taking ≤500 mg/day calcium

Additional Endpoints ≥4 weeks

- PRO* measures (HPES: a disease-specific PRO for HP)
- Nephrolithiasis, nephrosclerosis, vascular calcification, ER/urgent care visits and hospitalizations
- BMD and TBS by DXA, bone turnover markers, 24-hour urine calcium excretion (in extension only)

* PRO = patient-reported outcome

Simple Pen Injector in Phase 2

Key Features

- Simple operation
- Three multi-use pens with three different strengths (6, 9, 12 µg; 15, 18, 21 µg; 24, 27, 30 µg)
- Ready-to-use liquid formulation, room temp stability for 14 days
- Low injection volume (≤0.1 mL)
- Small (31G), short (5 mm) safety pen needle

Pen injector planned for commercial launch being used in phase 2

PaTHforward TRIAL

ascendis pharma

TransCon PTH: Highlights

- Phase 1 data support TransCon PTH as a true replacement therapy for HP
- Phase 2 trial initiated in adult HP subjects
  - Randomized placebo-controlled study for approximately four weeks with fixed TransCon PTH doses and titration regimen for complete withdrawal of SoC (active vitamin D and calcium)
  - Validation of disease-specific PRO for use in phase 3 trial
  - Introduction of ready-to-use prefilled pen device in the phase 2 trial
  - Subjects from phase 2 trial expected to enter into a long-term extension trial
- Phase 2 top-line data expected late Q4 2019
- On track to incorporate Asian territories into global phase 3 trial in late 2020

Hypoparathyroidism: A Story of Unmet Needs

Nyssa Noyola
VP, Strategic Planning & Project Management

Chronic Hypoparathyroidism: Significant Patient Population

Estimated Prevalence: ~200k in these 4 regions

USA

~70k-112k

- 2013, Powers et. al., Prevalence and Incidence of Hypoparathyroidism in the United States Using a Large Claims Database, JBMR
- 2011, Clarke et. al., Co-morbid Medical Conditions Associated with Prevalent Hypoparathyroidism: A Population-Based Study

Europe

~86k-223k

- 2013, Underbjerg et. al., Cardiovascular and Renal Complications to Postsurgical Hypoparathyroidism: A Danish Nationwide Controlled Historic Follow-up Study
- 2015, The Epidemiology of Nonsurgical Hypoparathyroidism in Denmark: A Nationwide Case Finding Study
- 2016, Astor et. al., Epidemiology and Health-Related Quality of Life in Hypoparathyroidism in Norway

Japan

~25k-32k

- 2016, Suzuki et. al., Factors Associated with Neck Hematoma After Thyroidectomy
- 2018, Interview conducted with Japanese HP expert

South Korea

~12k-13k

- S. Korean ICD-10 codes
- 2018, Interview conducted with S. Korean HP expert

Engaged Endocrinologists and Patients to Build Deeper Understanding of Hypoparathyroidism

2018 HP Survey (>100 Endocrinologists)

- Surveyed and interviewed >100 US endocrinologists treating patients with HP, across:
  - Private practice, teaching and non-teaching settings
  - Urban, suburban and rural settings
  - >30 US states
  - Varied patient volumes
  - Treatment preferences: prescribing SoC vs. PTH(1-84) vs. PTH(1-34)

2019 HP Patient Experience Research (>50 Patients)

- Interviewed >50[1] adult patients with HP
- Patient mix included:
  - Females and males, aged 26-76
  - Post-surgical and idiopathic HP
  - Suffering from HP for 1-49 years
  - Prescribed SoC and/or PTH replacement therapy

[1] Data analyses conducted using transcripts from 42 adult patients with HP, and HP Patient Experience Research also included cognitive debriefing with independent sample of 16 adult patients with HP

ascendis pharma

Endocrinologists Acknowledge Unmet Needs Remain[1]

Important Unmet Needs in Management of HP (N=108)

Absence of Long-Acting Therapy

> *A single dose of PTH preparation with long-enough half-life so that accidentally missing a dose does not place the patient in the [Emergency Department] in tetany*

Hypercalciuria

> *Urinary calcium and risk of nephrocalcinosis and kidney stones*

Absence of True Replacement Therapy

> *There is a need for a pathogenetic replacement drug that recapitulates and corrects all aspects of the syndrome, including the hypercalciuria*

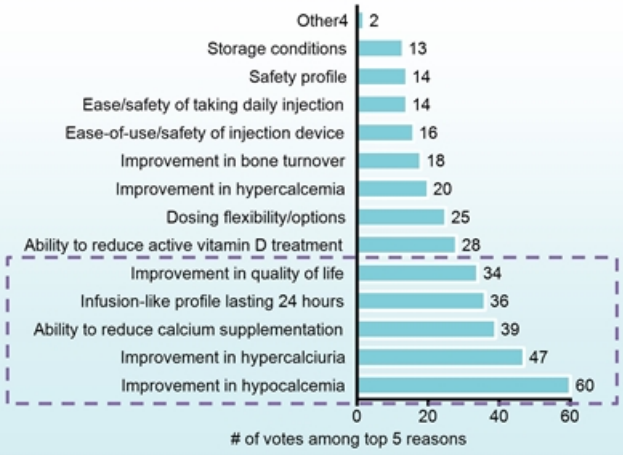
[1] Ascendis Pharma 2018 HP Survey; interviews conducted in Q2 2018; data on file

ascendis pharma

>70% of Physicians Indicate Likelihood to Prescribe TransCon™ PTH[1]

Physicians Likely to Prescribe TransCon PTH[2]
(N=108)

Reasons to Prescribe TransCon PTH[3,4]
(n=76)



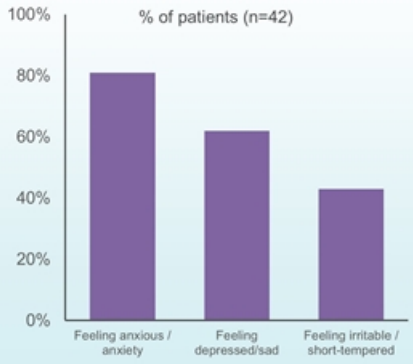
Confirms TransCon PTH target product profile and reinforces significant unmet need

[1] Ascendis Pharma 2018 HP Survey; interviews conducted in Q2 2018; data on file. [2] Respondents who selected 5-7 on 1-7 scale considered "likely to prescribe" TransCon PTH. [3] n=76 includes respondents likely to prescribe TransCon PTH. [4] Other includes Reduce serum phosphorus, Conserve renal function.

100% of Patients with Hypoparathyroidism Experience Negative Impacts[1]

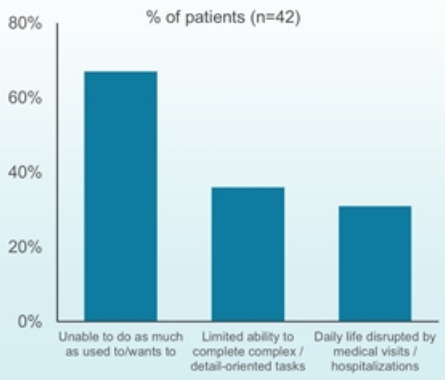
100% of Patients Reported Psychological Impacts

Psychological Impacts



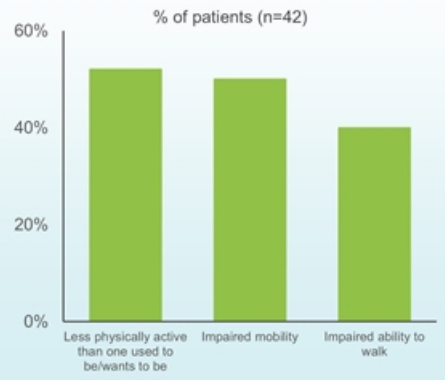
95% of Patients Reported Interference with Daily Life

Impacts on Daily Life



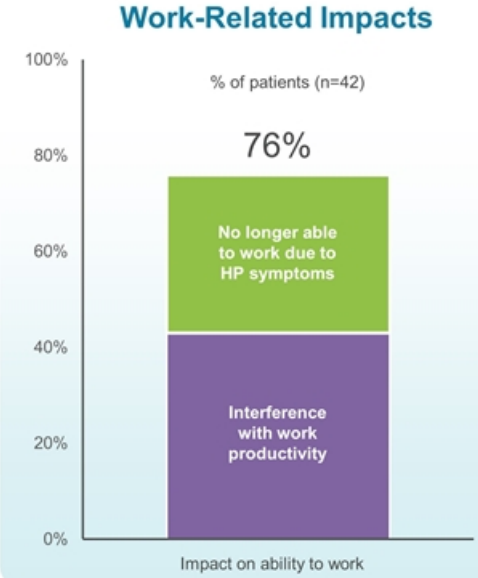
95% of Patients Reported Impacts on Physical Functioning

Impacts on Physical Functioning



[1] Poster presented at ENDO 2019 and 2019 Ascendis Pharma HP Patient Experience Research.

Vast Majority of Patients Unable to Work or Less Productive Due to HP Symptoms[1]



- Among those currently employed, 90% reported their HP symptoms interfered with work productivity, most often due to:
  - Ability to perform cognitive tasks
  - Absenteeism
  - Interference with ability to perform physical tasks
- 45% of patients experienced the economic impacts of a loss of income due to hypoparathyroidism

[1] Poster presented at ISPOR 2019 and 2019 Ascendis Pharma HP Patient Experience Research.

Majority of Patients Remain Unsatisfied with Current Management and Care for HP[1]

71% of Patients Reported Difficulty[2] in Managing HP

> *If my calcium level is good, then I might only have paresthesia four or five times a week. If I'm going through a really rough patch...then it will happen daily, several times a day. That's one of the things that can be very frustrating with this disease…it's so poorly controlled.*

64% of Patients Reported Difficulty to Find Physicians with Sufficient HP Knowledge

> *I find that doctors don't know much about this and...I have to educate them. I ordered these booklets from the hypoparathyroidism organization…The endocrinologist that I see he does have some patients that have hypoparathyroidism, but it's not the majority of his practice.*

[1] Poster presented at ISPOR 2019 and 2019 Ascendis Pharma HP Patient Experience Research.
[2] Somewhat, A Lot, or Extremely Difficult to Manage Their HP

ascendis pharma

Summary of Goals for TransCon PTH

TransCon PTH is designed to address all aspects of the disease by restoring physiological levels of PTH throughout the day

- Normalize serum and urinary calcium, eliminate active vitamin D supplementation and reduce calcium supplementation
- Address short-term and long-term complications of HP
- Improve quality of life by minimizing symptoms and impacts of disease
- Provide patients with easy-to-use, convenient pen injector

TransCon™ CNP: The New Frontier of Growth Biology

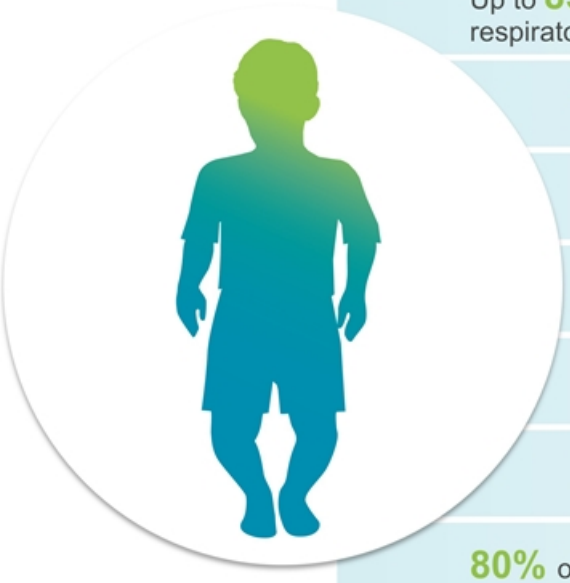
Kennett Sprogøe, Ph.D.
SVP, Innovation and Research

TransCon CNP: The New Frontier of Growth Biology

- C-type natriuretic peptide (CNP) is a promising therapeutic target for treating growth failure and dwarfism
  - Inhibits the overactive signalling resulting from both ligand-dependent and independent signalling through the mutated FGFR3 receptor causing achondroplasia
- Due to its very short half-life (2-3 minutes), CNP has historically not been a druggable target, as prolonged exposure is required for improved growth
- Phase 1 data support the TransCon CNP Target Product Profile

TransCon CNP may provide benefit in several growth disorders — as monotherapy, and potentially in combination with TransCon hGH

Achondroplasia: High Morbidity



Up to **85%** of patients require intervention for obstructive sleep apnea and respiratory insufficiency

25% of children have hearing loss increasing to > 50% in adulthood

22% have osteotomy

15-30% have fixed kyphotic deformity

Up to **28%** require cevicomedullary decompression by age 4

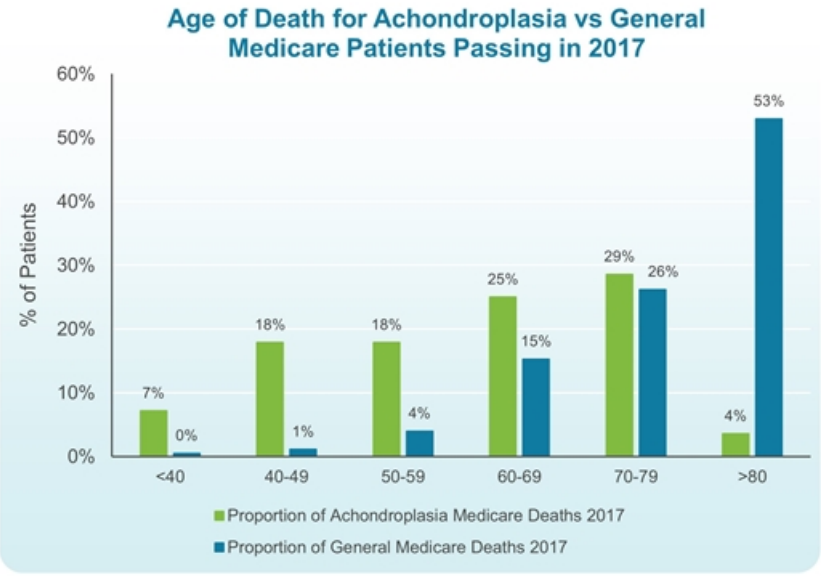
10% of children have neurological signs of spinal stenosis

80% of adults have clinical signs and symptoms related to spinal stenosis

Achondroplasia: Higher Mortality

Preliminary analysis shows among achondroplasia patients a median age of death of 60 years – consistent with the published literature

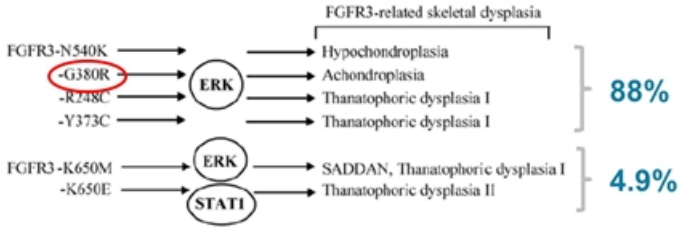
Markedly higher rates of death in these patients compared to the overall Medicare population, especially among patients <70 years



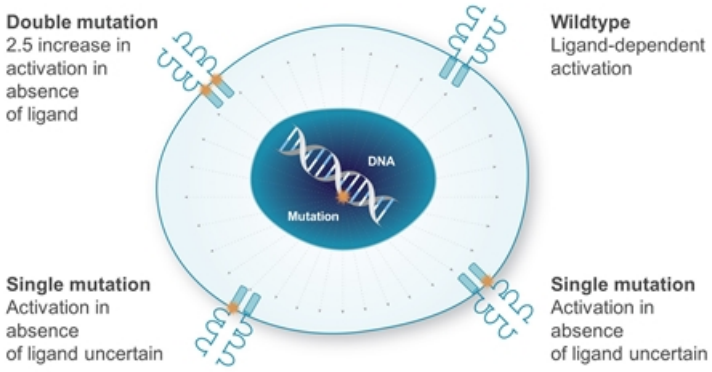
Analysis courtesy of Trinity Partners: Trinity Partners Medicare Analysis.
Results are preliminary and achondroplasia vs. overall Medicare patients have not been risk adjusted.

Achondroplasia: Autosomal Dominant Mutation in *FGFR3*

Mutations leading to different Skeletal Dysplasias[1]



Different Conformations of the FGFR3 G380R mutated dimer[2]



Downstream inhibition required to inhibit ligand-independent signaling

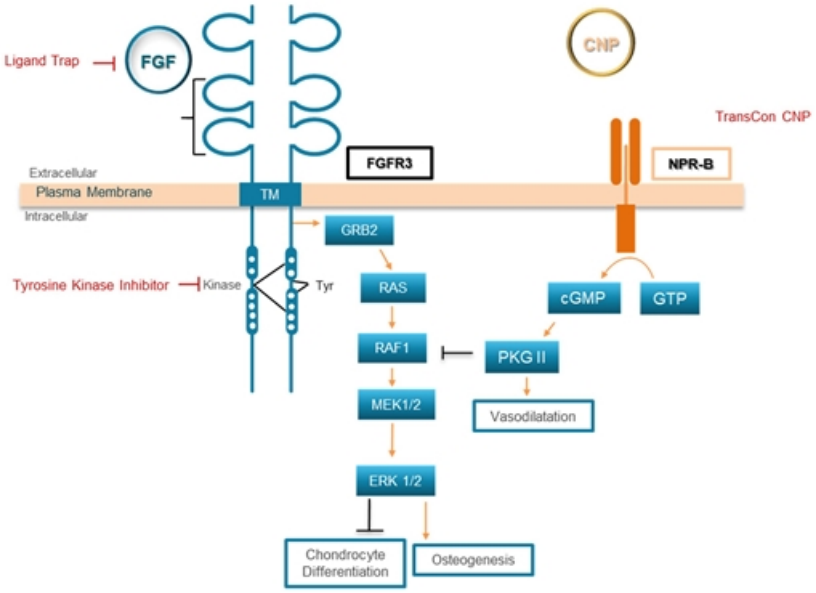
[1] Adapted from: PLoS ONE, 2008, 3(12), e3961
[2] J. Biological Chemistry, 285 pp 30103-30113

ascendis pharma

Achondroplasia Signaling Defect is Well Understood[1]

TransCon CNP continuously inhibits abnormal FGFR3 signaling, restoring proliferation and differentiation of chondrocytes to rebalance bone growth

CNP does not alter the function of FGF receptors or change endogenous levels of FGF ligands, reducing the risk of interfering with normal FGF biology



[1]Adapted from Current Opin Pediatrics 2010; 22:516-523

ascendis pharma

CNP: Fits Our Unique Algorithm for Innovation

To address the overactive FGFR3 signaling pathway, CNP was selected as the most promising target to rebalance growth

EFFICACIOUS

- Correction of phenotypical features in achondroplasia mouse model following continuous exposure to CNP

SPECIFICITY

- Only inhibiting abnormal FGFR3 signaling, and not interfering with other FGF biology

DEMONSTRATED SAFETY

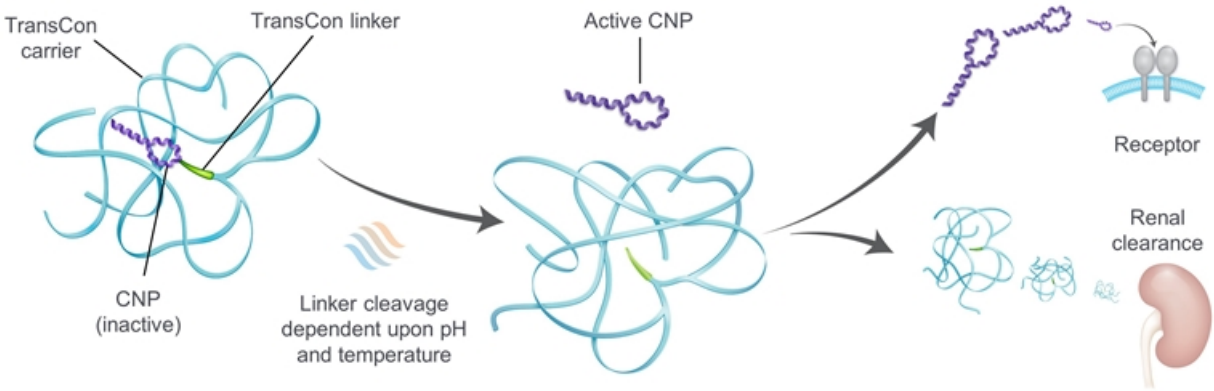
- Well-tolerated in clinical trials
- Overexpression in humans is associated with skeletal overgrowth, with no other associated adversity

ACCESS THE GROWTH PLATE

- Growth plate is an avascular tissue; restricts access from the blood stream
- Growth plate acting drugs must be systemically tolerated at higher concentrations than for local effects due to diffusion gradient

ascendis pharma

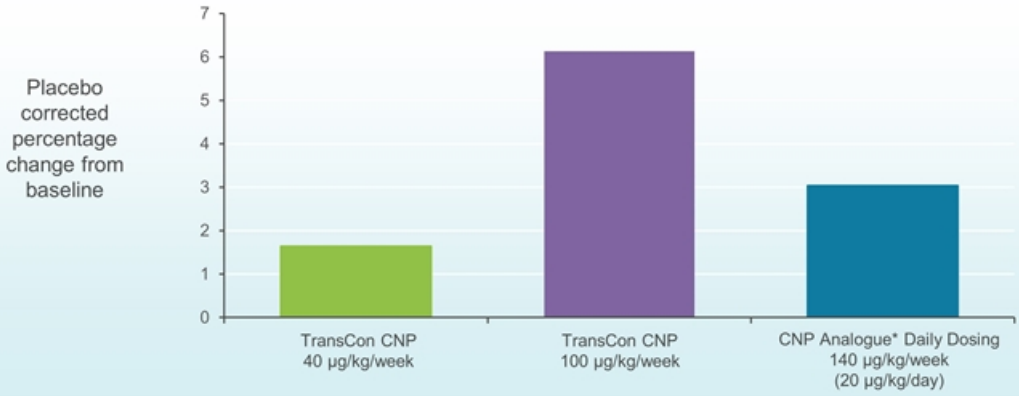
TransCon CNP Design



- TransCon technology is designed to provide effective shielding of CNP:
  - From neutral endopeptidase degradation in subcutaneous tissue and blood compartment
  - Minimize binding of TransCon CNP to the NPR-C receptor
  - Reduce binding of TransCon CNP to the NPR-B receptor in vasculature to avoid hypotension
- CNP liberated from TransCon CNP maintains small enough size to allow penetration into growth plates

Juvenile Healthy Monkey Growth Study

Tibial growth at 6 months (n=4/group)

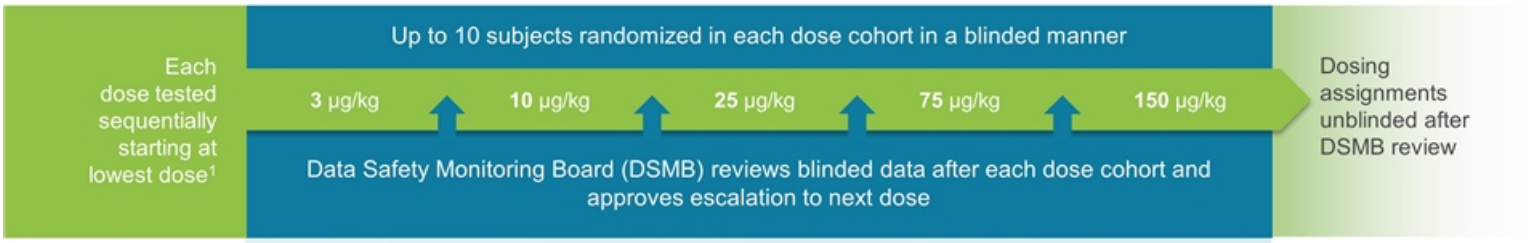


- Demonstrated dose-proportional tibial linear growth; ulnar growth consistent
- TransCon CNP induced a more robust growth response compared to daily administration of CNP, despite being administered at a 40% lower dose

* Refers to a synthesized molecule with a half-life of ~20 mins prepared by Ascendis Pharma

Phase 1 Trial Design

45 healthy adult male subjects
TransCon CNP vs. placebo (4:1 randomization)



Primary Endpoint

- Frequency of adverse events (AEs) reported after administration of TransCon CNP

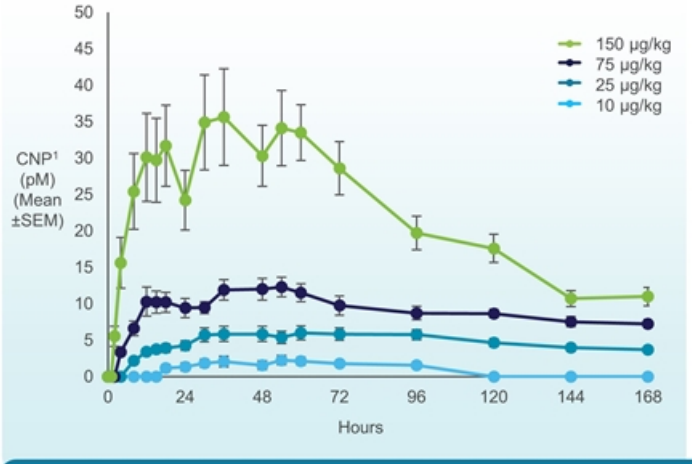
Secondary/Exploratory Endpoints

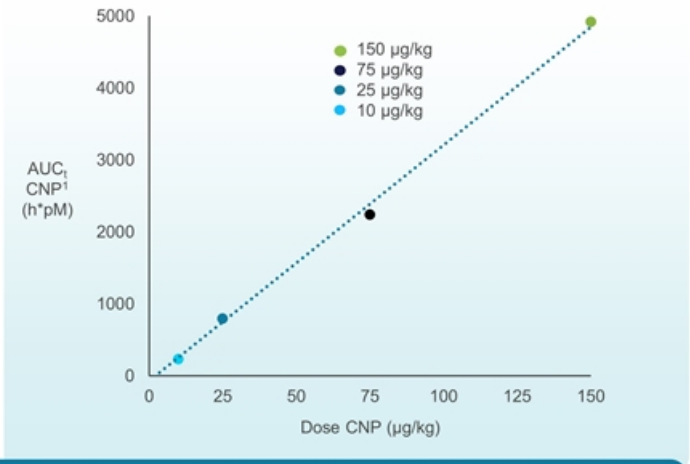
- Safety parameters and local tolerability assessment
- Pharmacokinetic parameters
- Other exploratory endpoints

[1] 300 µg CNP/kg cohort was deemed not clinically relevant based on emerging pharmacokinetic data from previous cohorts and therefore not dosed.

Dose Proportional CNP Exposure For 1 Week

TransCon CNP 10, 25, 75 and 150 µg/kg (n=5-8/group)





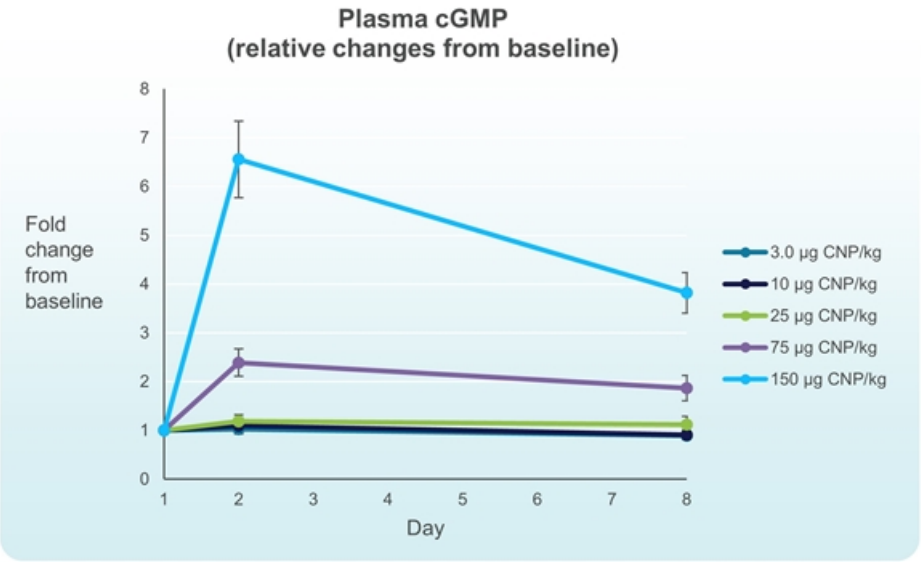
- Dose proportional increase in CNP exposure suggests ability to titrate dosing
- Phase 1 showed effective CNP $t_{1/2}$ of approximately 120 hours (native CNP $t_{1/2}$ of 2-3 minutes)

[1] CNP measured as CNP-38

ascendis pharma

Dose Dependent cGMP[1] Response Demonstrated Receptor Engagement For 7 Days

- cGMP is a secondary messenger of NPR-B activation by CNP
- cGMP levels correlate with TransCon CNP PK profile



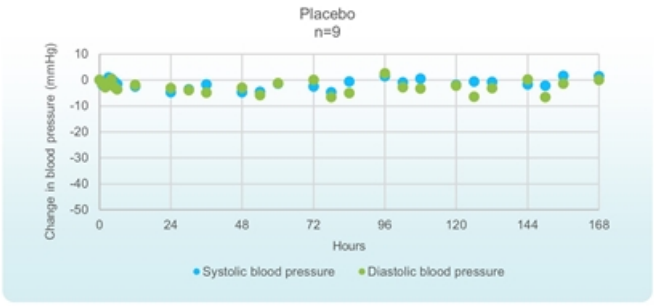
[1] cGMP=cyclic guanosine monophosphate.

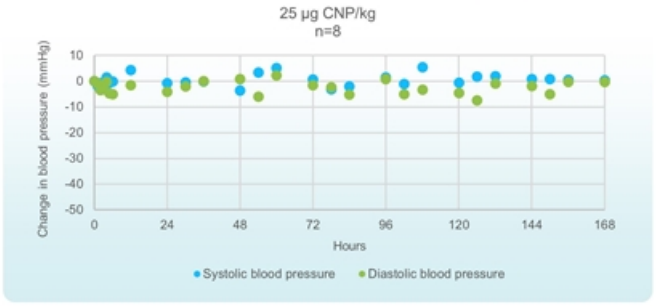
No Downregulation of Endogenous CNP Production

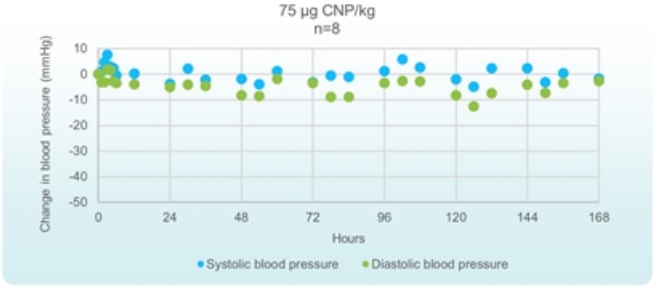
- The amino-terminal propeptide (NTproCNP[1]) of CNP is a marker of endogenous CNP biosynthesis
- Across dose cohorts, no changes in NTproCNP levels were observed upon exposure
- No impact on CNP biosynthesis observed following single dose administration of TransCon CNP in healthy adults

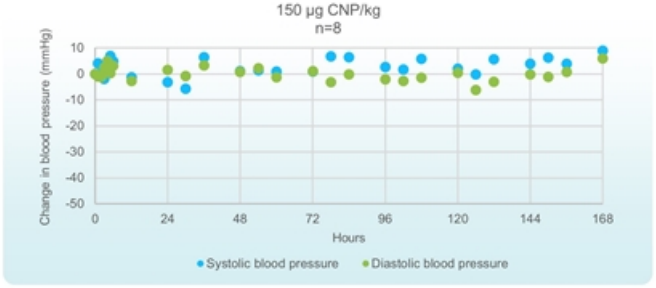
[1] NTproCNP=N-Terminal Pro CNP

Mean Resting Blood Pressure Unchanged from Predose[1]









Change in systolic blood pressure Change in diastolic blood pressure

[1] 3.0 and 10 µg/kg dose levels are not represented. Data from these cohorts are consistent with placebo.

TransCon CNP: Well-tolerated Safety Profile

- No serious AEs were reported in the trial
- TransCon CNP was generally well tolerated at doses up to 150 µg/kg
- No anti-CNP antibodies detected in any subjects
- Mean resting blood pressure and heart rate were unchanged from pre-dose at all time points, in all cohorts
- Mean orthostatic changes in vital signs appear unrelated to TransCon CNP exposure; consistent between placebo and TransCon CNP cohorts
- Injections were well tolerated in all dose cohorts

ACHieve Ongoing and Enrolling

ACHieve STUDY

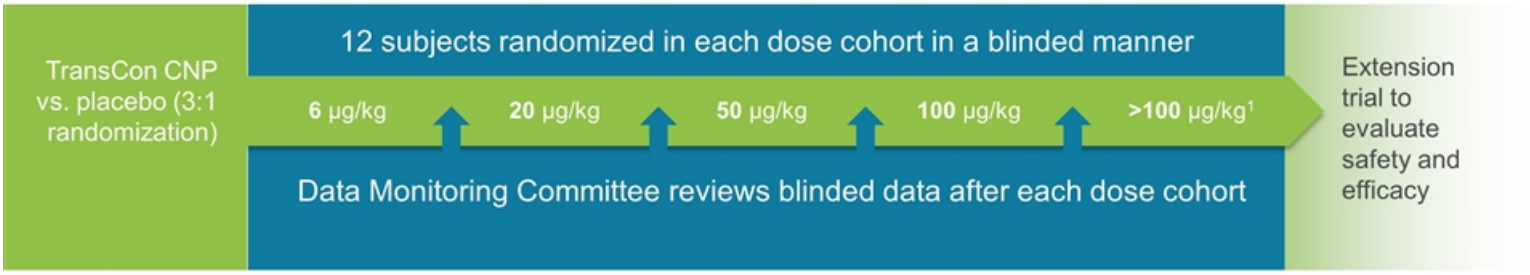
- A global natural history study of ~200 children <8 years with achondroplasia (ACH)
- Evaluates height velocity, body proportionality and comorbidities
- Establishes relationships with study sites worldwide, paving the way for potential future TransCon CNP clinical trials
- Twenty sites selected:
  - Australia, Austria, Canada, Germany, Ireland, Italy, Portugal, Spain, Switzerland, UK, and US
  - Site qualification ongoing in other potential countries

ascendis pharma

TransCon CNP: Preliminary Phase 2 Trial Design

ACcomplisH TRIAL

Up to 60 children (ages 2 – 10 years) with achondroplasia



Primary Endpoint

- Annualized height velocity, as measured after 12 months of weekly TransCon CNP treatment

Key Secondary Endpoints

- Change in body proportionality (upper to lower body segment ratio), as measured after 12 months of weekly TransCon CNP treatment
- Change in body mass index (BMI), as measured after 12 months of weekly TransCon CNP treatment
- Patient reported outcome (PRO) measures

[1] Dose to be determined. If needed, based on emerging data.

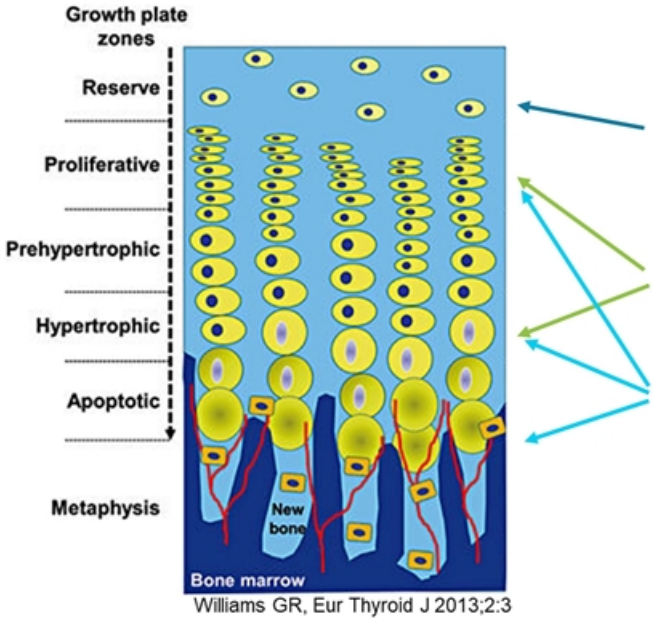
ascendis pharma

Expanding the Treatment Paradigm in Growth Disorders

TransCon hGH and TransCon CNP represent potential best-in-class product opportunities that we believe can be combined to improve treatment of growth disorders

Several growth disorders may benefit from combination therapy, including skeletal dysplasias, idiopathic short stature (ISS) and small for gestational age (SGA)

Growth Biology: Rationale for Combination Effects of Different Pathways



Williams GR, Eur Thyroid J 2013;2:3

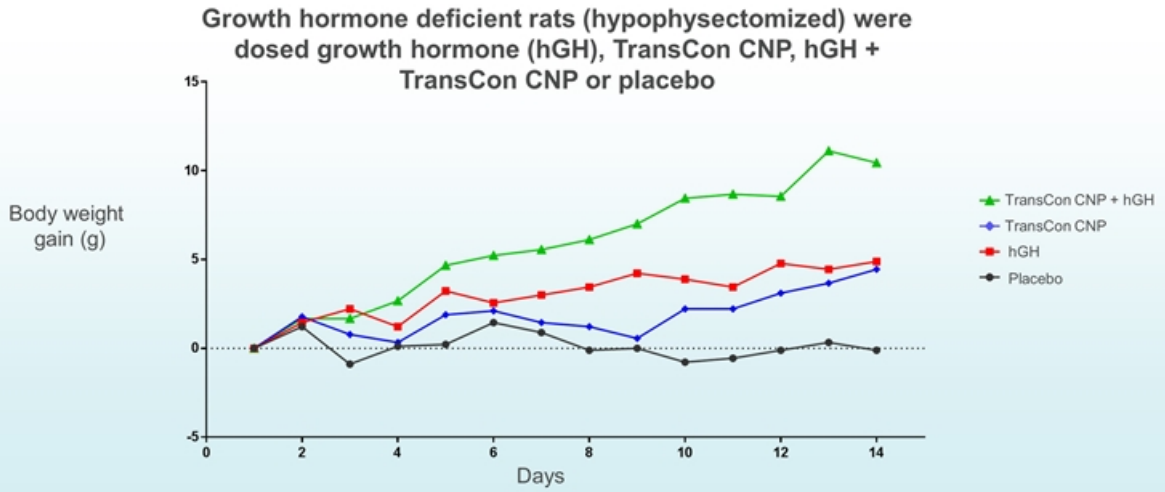
hGH acts directly on pre-chondrocytes in the growth plate, driving differentiation into chondrocytes required for sustained growth. hGH also stimulates local production of IGF-1

IGF-1 stimulates chondrocyte proliferation, hypertrophy and survival

CNP stimulates chondrocyte proliferation, hypertrophy, differentiation, and increases in extracellular matrix formation

Sources: Endocrine Reviews 1987 8 426–438. Endocrine Connections (2018) 7, R212–R222. J Mol Endocrinol. 2014; 53(1): T1–T9.

Additive Effects of hGH and TransCon CNP



Additive effect of combining of TransCon CNP and hGH consistent with stimulation of different signaling pathways in the growth plate

TransCon CNP: Highlights

- TransCon CNP phase 1 data reproduced PK profile and cardiovascular safety from preclinical studies, providing continuous CNP exposure over seven days with a single subcutaneous administration
  - Continuous CNP exposure at target levels is important for balancing the CNP/FGFR3 pathways and normalizing growth
  - Generally well tolerated across all cohorts
  - No anti-CNP antibodies in any subject
- Potential for a significant impact on patients' lives, not only affecting height but also addressing many comorbidities associated with achondroplasia
- ACHieve STUDY (natural history study) ongoing; initiation of phase 2 ACcomplisH TRIAL expected Q3 2019
- Potential to expand into other growth disorders as monotherapy and combined with TransCon hGH
- Multiple patent concepts provide potential protection into 2037

TransCon PTH & TransCon CNP

Summary and Q&A

TransCon PTH: Developing a True Replacement Therapy

- Phase 1 data support infusion-like profile of TransCon PTH as a true replacement therapy for HP, building on established approach to treat short-term symptoms and long term complications
- PaTH Forward phase 2 trial initiated in adult HP subjects with simple ready-to-use injector pens, followed by long-term extension trial; top-line data expected Q4 2019
- On track to initiate global phase 3 trial in H2 2020 in North America, Europe and Asia
- >70% of endocrinologists[1] indicated likelihood to prescribe TransCon PTH if approved
- ~65% of patients reported difficulty finding physicians with sufficient HP knowledge; disease education needed
- Disease burden validates potential market opportunity for TransCon PTH as potential best-in-class therapy for solving unmet need

[1] Ascendis Pharma 2018 HP Survey; interviews conducted in Q2 2018; data on file

TransCon CNP: Pursuing New Frontier of Growth Biology

- Patients with achondroplasia (ACH) suffer numerous comorbidities, shorter lifespan and reduced quality of life; no FDA-approved therapy exists
- Selected CNP as preferred mode of action to treat disease, given necessity for downstream inhibition
- Preclinical findings and phase 1 data support TransCon CNP as providing continuous CNP exposure to balance CNP/FGFR3 pathways and restore growth
- Phase 1 data also demonstrated safety: well-tolerated with no serious AEs, no impact on blood pressure or heart rate, no downregulation of endogenous CNP production, and no anti-CNP antibodies
- Potential for significant impact on patients' lives, affecting height and many comorbidities associated with disease
- ACHieve natural history study enrolling; initiation of ACcomplisH phase 2 trial expected Q3 2019
- Potential to pursue other growth disorders as monotherapy and in combination with TransCon hGH

Q & A

Oncology

Juha Punnonen, MD, PhD
SVP, Head of Oncology

Today's Agenda

9:00-9:05 a.m.	**Welcome & Agenda Overview** Scott T. Smith
9:05-9:15 a.m.	**Vision 3x3** Jan Møller Mikkelsen
9:15-9:30 a.m.	**TransCon Platform & Product Innovation** Kennett Sprogøe, Ph.D.
9:30-10:05 a.m.	**TransCon hGH** Jonathan Leff, M.D.
10:05-10:15 a.m.	**Connected Healthcare Platform** Thomas Ørts Pedersen
10:15-10:30 a.m.	**Commercialization Update** Tom Larson
10:30-10:40 a.m.	**Q&A: TransCon hGH**
10:40-10:50 a.m.	**Break**
10:50-11:20 a.m.	**TransCon PTH** David Karpf, M.D. & Nyssa Liebermann Noyola
11:20-11:35 a.m.	**TransCon CNP** Kennett Sprogøe, Ph.D.
11:35-11:45 a.m.	**Q&A: TransCon PTH & TransCon CNP**
11:45-12:05 p.m.	**Introducing Oncology** Jan Møller Mikkelsen & Juha Punnonen, M.D., Ph.D.
12:05-12:20 p.m.	**IO & IT Treatments: Challenges & Promise** Ezra Cohen, M.D.
12:20-12:40 p.m.	**Oncology Product Candidates** Juha Punnonen, M.D., Ph.D.
12:40-12:50 p.m.	**Q&A: Oncology**
12:50-1:00 p.m.	**General Q&A & Closing Remarks** Jan Møller Mikkelsen

ascendis pharma

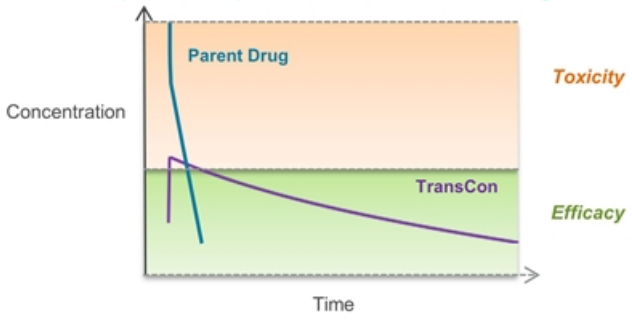
Vision in Oncology

- Create best-in-class oncology therapies by applying systemic and intratumoral TransCon™ technologies for clinically validated pathways
- Improve outcomes upon validated mechanisms that are currently limited by suboptimal efficacy and systemic toxicity
  - Apply Ascendis' unique algorithm for product innovation to oncology development
- Build a diversified high-value pipeline addressing multiple indications
  - File first IND (or equivalent) in 2020
- Enable rapid path to global commercialization, including through mutually-beneficial collaborations as needed

Positioned to Make a Dramatic Impact in Oncology

- Aiming to apply TransCon technologies to clinically validated mechanisms to develop differentiated and potentially best-in-class products
  - Large number of validated oncology targets with known limitations
  - Applicable for diverse drug classes and mechanisms of action
  - Enable both systemic and intratumoral (IT) approaches

Expected Impact of TransCon Technologies

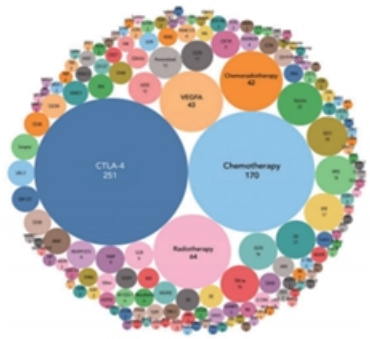


Potential to enable superior efficacy of small molecules, peptides, proteins without increased toxicity by prolonging therapeutic levels

ascendis pharma

TransCon Has the Potential to Address the Toxicity Challenges Associated with Multi-agent Combination Treatments

Large Number of Combination Trials Ongoing



Tang et al., Ann Onc, 2018

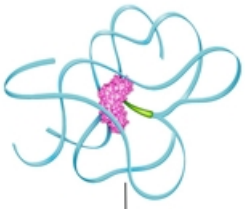
Combinations Have Gained Recent FDA-Approvals, while Combination Toxicity and Treatment Discontinuations are Limiting Success

	PD-1 mono-therapy[1,2]	PD-1 + chemotherapy[3]	PD-1 + VEGF-TKI[4]	PD-1 + CTLA-4[5]
Grade 3 or 4 AE[6]	10%	67%	76%	59% (TRAE[7])
AEs leading to discontinuations	2 – 12%	20%	30%	39%

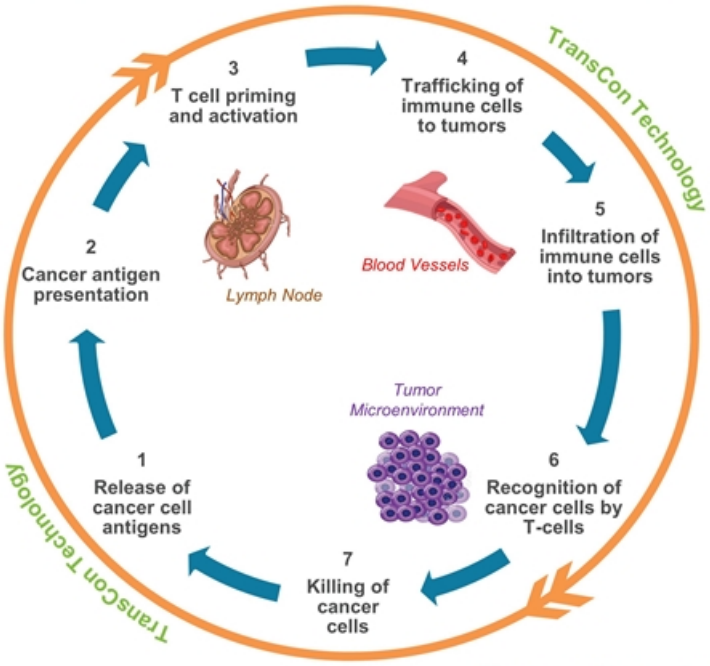
TransCon technologies have the potential to enable new multi-agent combinations with lower toxicity than feasible with approved approaches

[1] N Engl J Med 2015, 372(21);1673-1682. [2] J Clin Oncol 2017, 35:7; 785-792. [3] N Engl J Med 2018, 378(22); 2078-2092. [4] N Engl J Med 2019; 380; 1116-1127. [5] N Engl J Med 2017; 377(14);1345-1356.
[6] AE = adverse event. [7] TRAE = treatment related adverse event

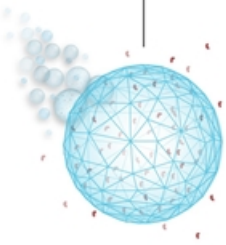
Potential to Broadly Facilitate in Anti-tumor Responses: *TransCon Immunity Cycle*



TransCon: Sustained systemic delivery



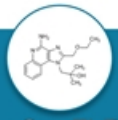
TransCon: Sustained intratumoral delivery



Differentiated Product Opportunities via Systemic or IT Routes

TransCon IL-2 β/γ

- Designed to preferentially activate $CD8^+$ T and NK cells relative to Treg cells
- TransCon sustained systemic delivery



TransCon TLR 7/8 Agonist

- Designed to enhance innate immune response and antigen presentation
- TransCon sustained intratumoral delivery

TransCon VEGF-TKI

- Designed to modulate tumor microenvironments to facilitate immune response
- TransCon sustained intratumoral delivery

IL-2 = Interleukin-2; image adapted from Ring et al., Nat Immunol, 13: 1187, 2012; TLR = Toll-like Receptor; VEGF-TKI = Vascular Endothelial Growth Factor-Tyrosine Kinase Inhibitor

ascendis pharma

Product Candidates in Oncology

IL-2 Selective for the IL-2Rβ/γ

TransCon
IL-2 β/γ

Opportunity for TransCon IL-2 β/γ

Efficacy
- Sustained release of IL-2 with selectivity for β/γ receptor is needed to improve exposure and activation of CD8+ T cells and NK cells relative to Tregs

Safety
- Sustained release of selective IL-2 expected to avoid high Cmax and reduce risk of vascular leak syndrome

New Indications
- Improved tolerability is needed to enable more aggressive combination approaches
- Potential efficacy across multiple indications

TransCon IL-2 β/γ

Designed to achieve optimal ***receptor binding*** and ***exposure profile*** for ***superior efficacy and tolerability***

ascendis pharma

IL-2: Validated Cytokine with Suboptimal Receptor Binding *and* PK Properties

Suboptimal receptor binding

- Two receptors: IL-2Rα/β/γ and IL-2Rβ/γ
- α/β/γ receptor activates Tregs and endothelial cells, reducing efficacy and increasing risk of capillary leak syndrome

Suboptimal PK

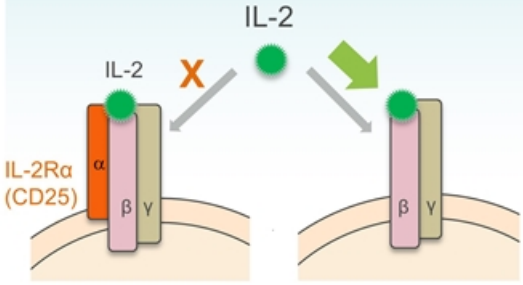
- Short half life of IL-2 (~1.5 h)
- High Cmax and pulsatile dosing drive adverse events

- Several IL-2 approaches in development
- To our knowledge, none have fully solved both shortcomings of IL-2

ascendis pharma

Next Generation IL-2: Designed for Desired Receptor Binding and Exposure

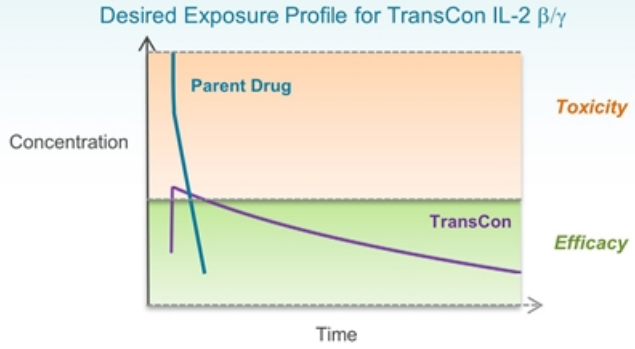
1 Prevent IL-2Rα binding to selectively activate β/γ receptor



Promotes Treg → Limit anti-tumor responses

Promotes CD8⁺ → Promote anti-tumor responses

2 Generate a product with long-lasting exposure avoiding high Cmax



153 | Figure adapted from Onur et al., Biomed Intell, 2019

All product candidates are investigational. For investor communication only. Not for use in promotion.

ascendis pharma

Design of IL-2 β/γ: Site-selective PEGylation for Permanent Receptor Selectivity and Optimized Potency

Generation of IL-2 Variant

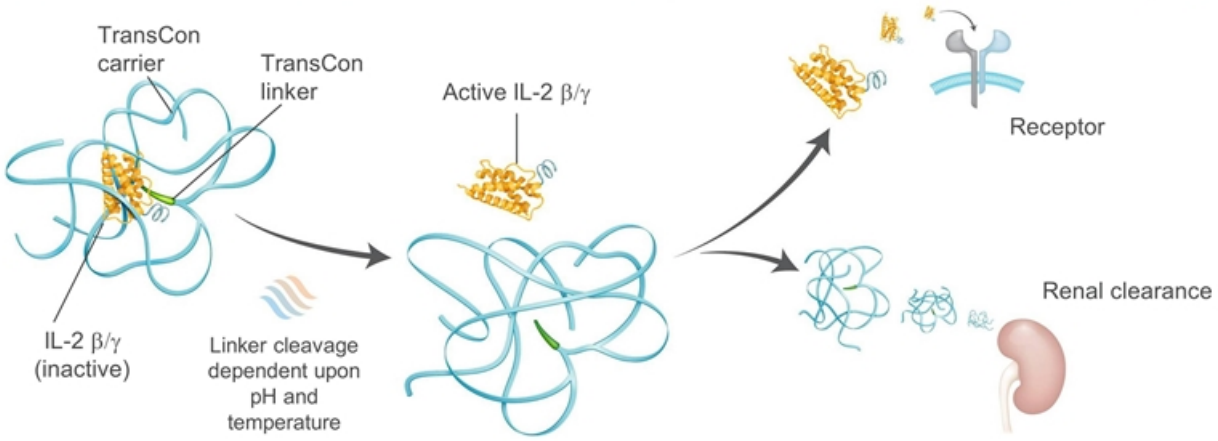
Introduction of cysteine at α–binding site of IL-2

Blocking α–binding

Site-selective permanent conjugation of small (<10kDa) PEG molecule results in selective binding to IL-2Rβ/γ

ascendis pharma

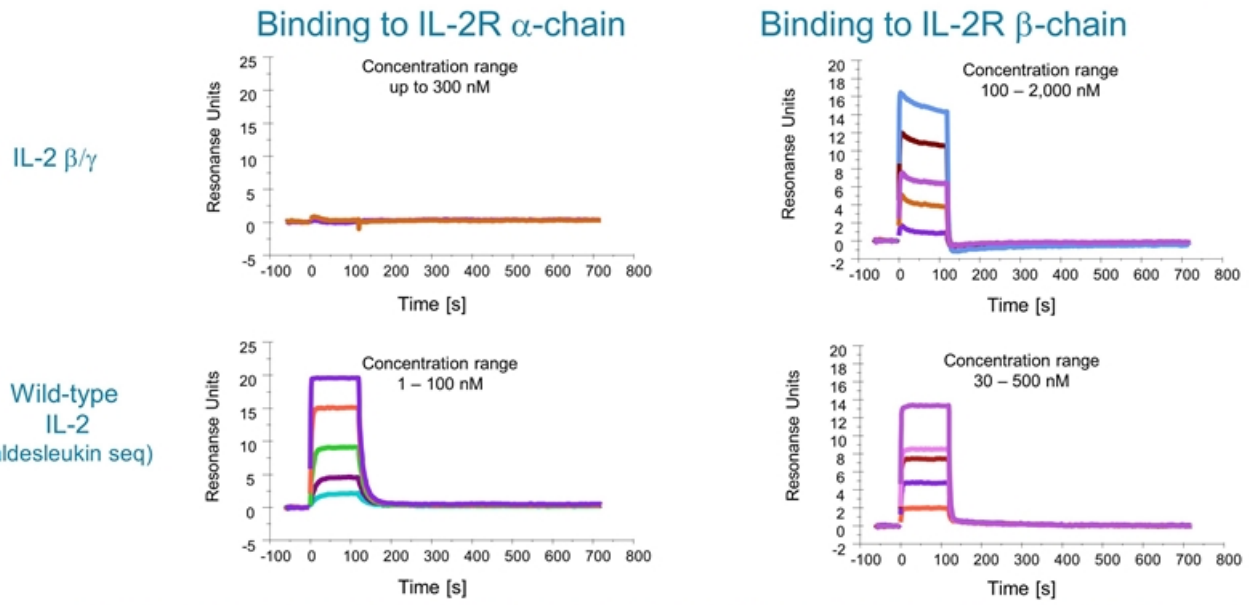
Design of TransCon IL-2 β/γ



TransCon Technology designed to generate long-acting, permanently receptor selective TransCon IL-2 β/γ

- ✓ Prevent IL-2Rα binding to selectively activate β/γ receptor
- ✓ Sustained, long-lasting exposure utilizing the TransCon hGH linker and carrier, predicted to have a half-life in humans of 2-3 days

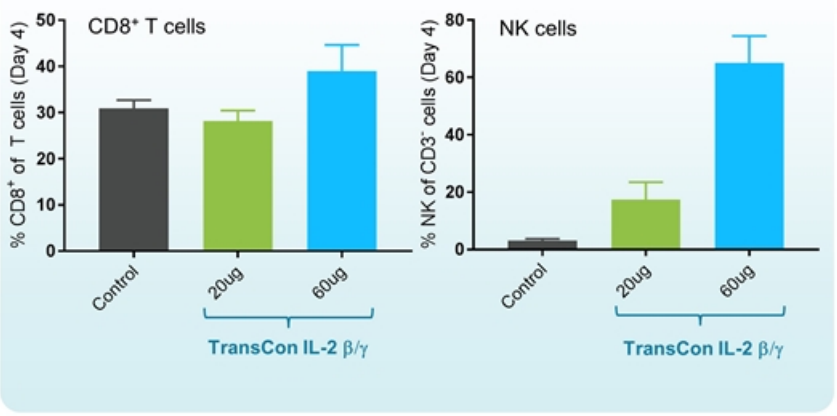
Permanently PEGylated IL-2 β/γ Demonstrated Low Binding to IL-2Rα, while Retaining Binding to IL-2Rβ



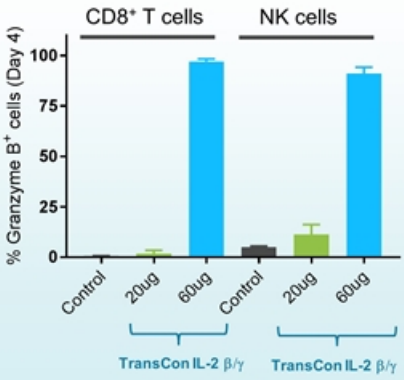
Receptor selectivity confirmed in cell-based assays, including primary human Tregs and CD8⁺ T cells

TransCon IL-2 β/γ Expanded and Activated CD8+ T cells and NK Cells *in vivo* in Mice

TransCon IL-2 β/γ Expanded CD8+ T cells and NK Cells *in vivo*

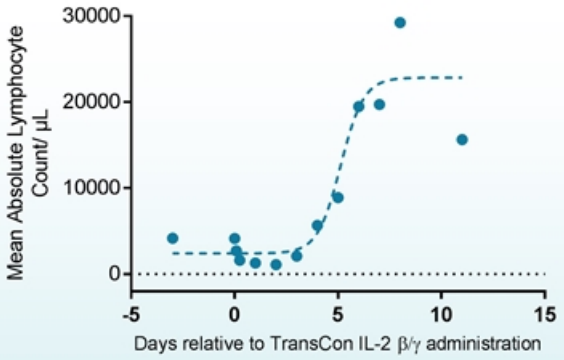


TransCon IL-2 β/γ Activated Both CD8+ T cells and NK cell *in vivo*

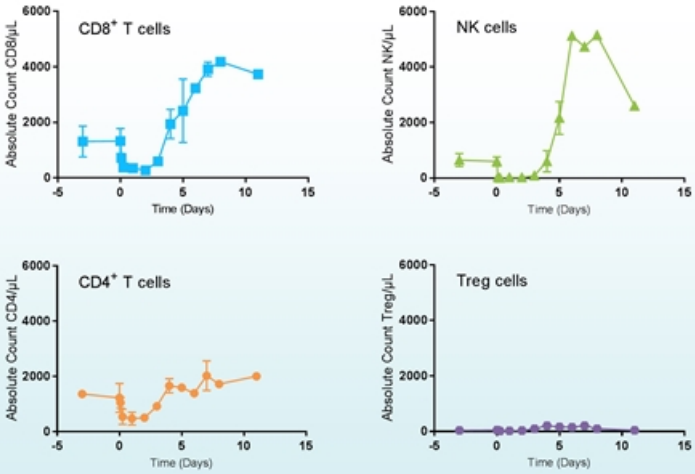


ascendis pharma

Single Dose of TransCon IL-2 β/γ Increased Levels of Circulating CD8+ T cells and NK cells in Cynomolgus Monkeys



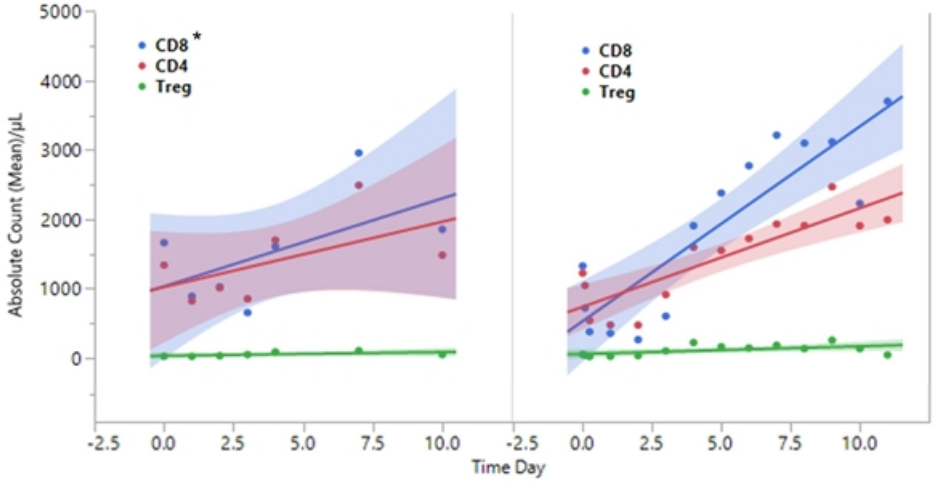
Compound Name	Sex/Weight	Dose (*mg/animal*)	Dosing frequency
TransCon IL-2 β/γ	M/9.2 kg M/8.9 kg M/9.0 kg	0.5 1.0 1.5	Once on Day 0



TransCon IL-2 β/γ Preferentially Expanded CD8+ T cells Relative to Treg cells in Cynomolgus Monkeys

Three doses of Aldesleukin IV (0.4 mg/animal/dose)

Single Dose of TransCon IL-2 β/γ IV (0.5 – 1.5 mg/animal)



TransCon IL-2 β/γ well tolerated:

- No dose-limiting toxicity
- No changes in clinical chemistry parameters (albumin, globulin, creatinine, ALT, AST, bilirubin)

Compound Name	Sex /Weight	Dose (*mg/animal*)	Dosing frequency
Aldesleukin	M/8.3 kg M/8.2 kg	0.4 0.4	Days 0, 1, 2 Days 0, 2, 4
TransCon IL-2 β/γ	M/9.2 kg M/8.9 kg M/9.0 kg	0.5 1.0 1.5	Once on Day 0

*Numbers of peripheral blood CD4+ T cells, CD8+ T cells, and Treg cells (CD4+, CD25+, FOXP3+) were analyzed by flow cytometry. Linear regression line with 95% confidence intervals is shown.

ascendis pharma

TransCon IL-2 β/γ - Summary

- Designed to fully solve the limitations of IL-2
  - Optimized receptor binding and exposure
  - Selective activation of IL-2Rβ/γ observed
  - Potent expansion and activation of $CD8^+$ T cells and NK cells *in vivo*
  - Preferential activation of $CD8^+$ T cells relative to Tregs observed in cynomolgus monkeys with a single dose
  - TransCon IL-2 β/γ was well-tolerated with no dose limiting toxicity and no clinical chemistry parameters measured
- Potential for best-in-class IL-2 molecule across multiple tumor types

Immunotherapy of cancer and intratumoral treatments: challenges and promise

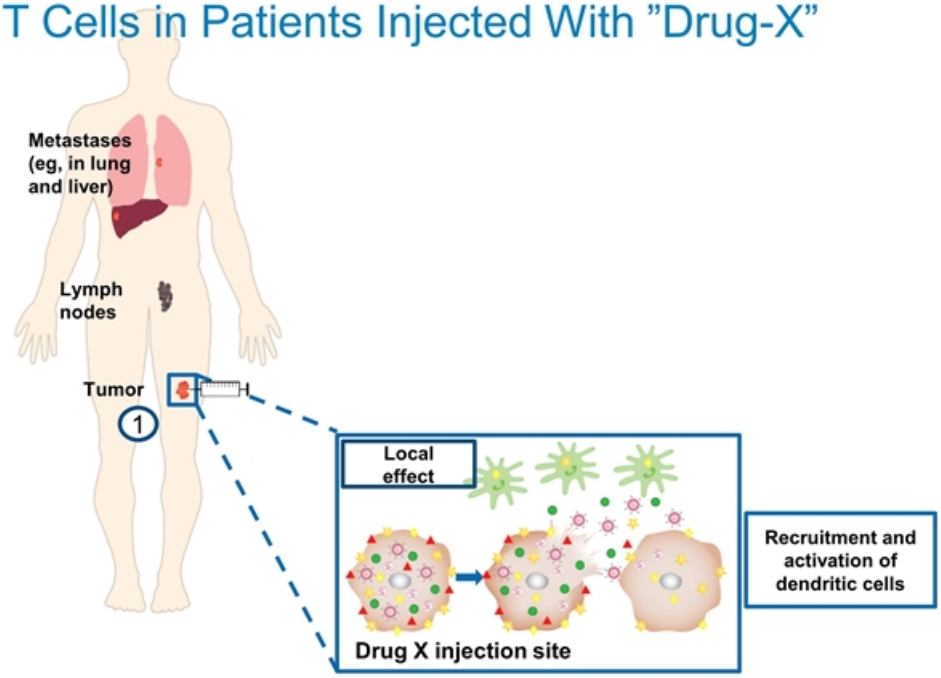
NCI CCC
A Comprehensive Cancer Center Designated by the National Cancer Institute

Ezra E. Cohen, MD

Rationale for Intra-tumoral Injection

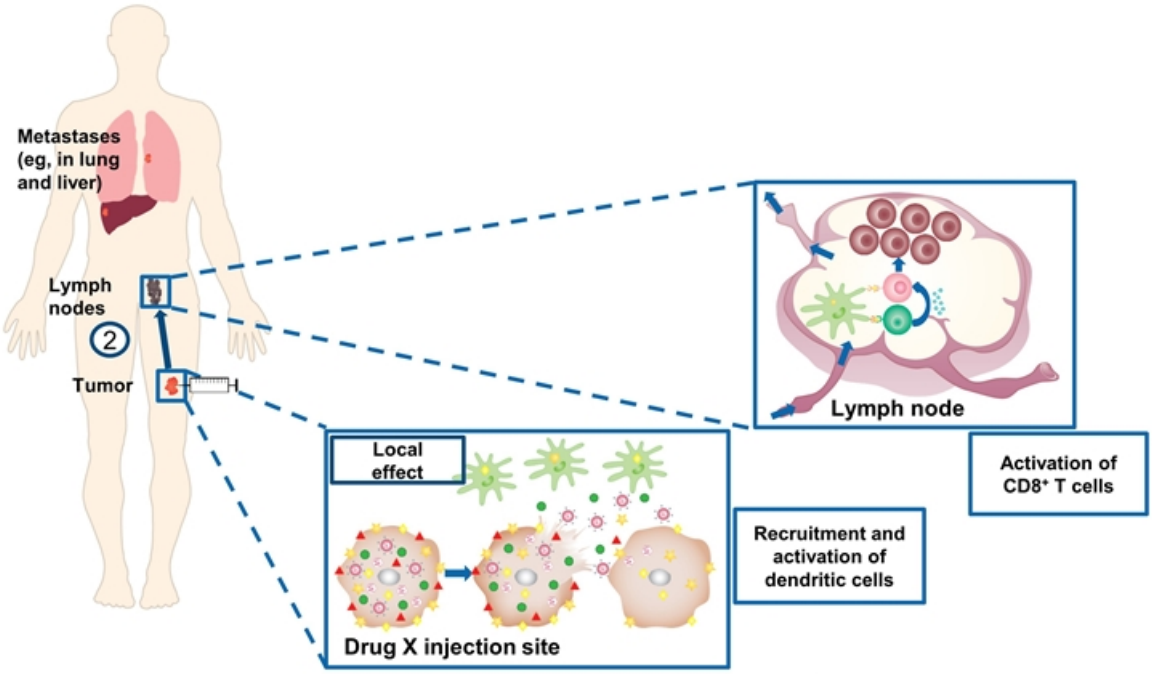
- Allows direct administration of agent to cellular targets
- Avoidance of systemic toxicity – greater therapeutic window
- Can avoid immune tolerance

Local Immune Activation and Systemic Tumor-Cell Killing by Activated CD8+ T Cells in Patients Injected With "Drug-X"



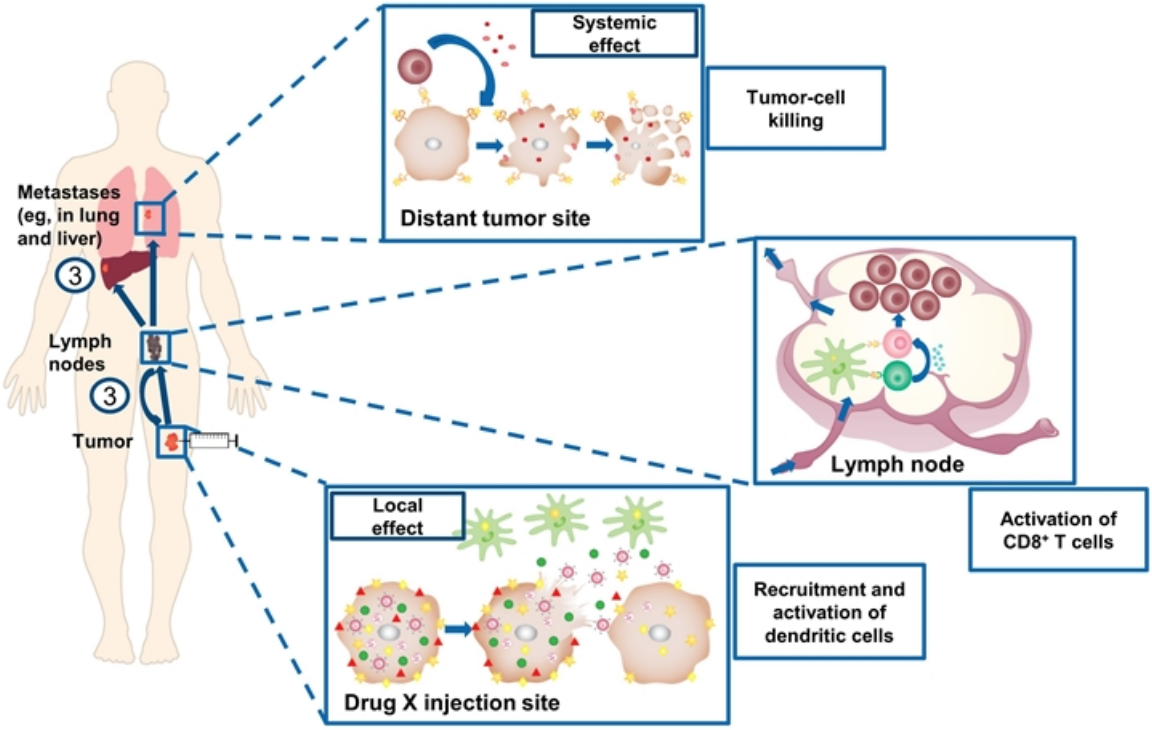
Toda M, et al. *Mol Ther*. 2000;2(4):324-239. Hawkins LK, et al. *Lancet Oncol*. 2002;3(1):17-26. Varghese S, et al. *Cancer Gene Ther*. 2002;9(12):967-978. Dranoff G. *Oncogene*. 2003;22(20):3188-3192. Liu BL, et al. *Gene Ther*. 2003;10(4):292-303. Eager R, et al. *Mol Ther*. 2005;12(1):18-27. Hu JC, et al. *Clin Cancer Res*. 2006;12(22):6737-6747. Fukuhara H, et al. *Curr Cancer Drug Targets*. 2007;7(2):149-155. Finn O. *N Engl J Med*. 2008;358(25):2704-2715. Melcher A, et al. *Mol Ther*. 2011;19(6):1008-1016. Sobol PT, et al. *Mol Ther*. 2011;19(2):335-344. Palucka K, et al. *Nat Rev Cancer*. 2012;12(4):265-277. Senzer NN, et al. *J Clin Oncol*. 2009;27(34):5763-5771. Clough KB, et al. *Ann Surg Oncol*. 2010;17(5):1375-1391. Andtbacka RH, et al. *J Clin Oncol*. 2013;31(suppl): Abstract LBA9008.

UC San Diego Health



Toda M, et al. *Mol Ther*. 2000;2(4):324-239. Hawkins LK, et al. *Lancet Oncol*. 2002;3(1):17-26. Varghese S, et al. *Cancer Gene Ther*. 2002;9(12):967-978. Dranoff G. *Oncogene*. 2003;22(20):3188-3192. Liu BL, et al. *Gene Ther*. 2003;10(4):292-303. Eager R, et al. *Mol Ther*. 2005;12(1):18-27. Hu JC, et al. *Clin Cancer Res*. 2006;12(22):6737-6747. Fukuhara H, et al. *Curr Cancer Drug Targets*. 2007;7(2):149-155. Finn O. *N Engl J Med*. 2008;358(25):2704-2715. Melcher A, et al. *Mol Ther*. 2011;19(6):1008-1016. Sobol PT, et al. *Mol Ther*. 2011;19(2):335-344. Palucka K, et al. *Nat Rev Cancer*. 2012;12(4):265-277. Senzer NN, et al. *J Clin Oncol*. 2009;27(34):5763-5771. Clough KB, et al. *Ann Surg Oncol*. 2010;17(5):1375-1391. Andtbacka RH, et al. *J Clin Oncol*. 2013;31(suppl): Abstract LBA9008.

UC San Diego Health



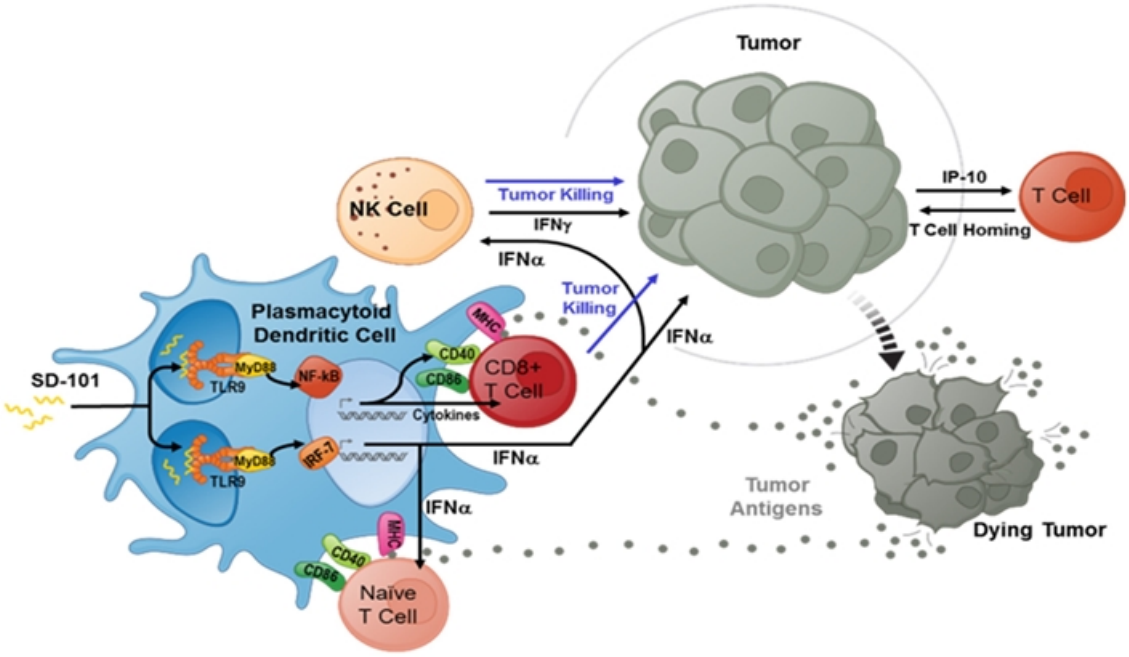
Toda M, et al. *Mol Ther*. 2000;2(4):324-239. Hawkins LK, et al. *Lancet Oncol*. 2002;3(1):17-26. Varghese S, et al. *Cancer Gene Ther*. 2002;9(12):967-978. Dranoff G. *Oncogene*. 2003;22(20):3188-3192. Liu BL, et al. *Gene Ther*. 2003;10(4):292-303. Eager R, et al. *Mol Ther*. 2005;12(1):18-27. Hu JC, et al. *Clin Cancer Res*. 2006;12(22):6737-6747. Fukuhara H, et al. *Curr Cancer Drug Targets*. 2007;7(2):149-155. Finn O. *N Engl J Med*. 2008;358(25):2704-2715. Melcher A, et al. *Mol Ther*. 2011;19(6):1008-1016. Sobol PT, et al. *Mol Ther*. 2011;19(2):335-344. Palucka K, et al. *Nat Rev Cancer*. 2012;12(4):265-277. Senzer NN, et al. *J Clin Oncol*. 2009;27(34):5763-5771. Clough KB, et al. *Ann Surg Oncol*. 2010;17(5):1375-1391. Andtbacka RH, et al. *J Clin Oncol*. 2013;31(suppl): Abstract LBA9008.

UC San Diego Health

Challenges for Intra-tumoral Injection

- Access
  - Limits patient population or requires interventional expertise
- Need for relatively frequent and regular injections
- Potential for vascular injury

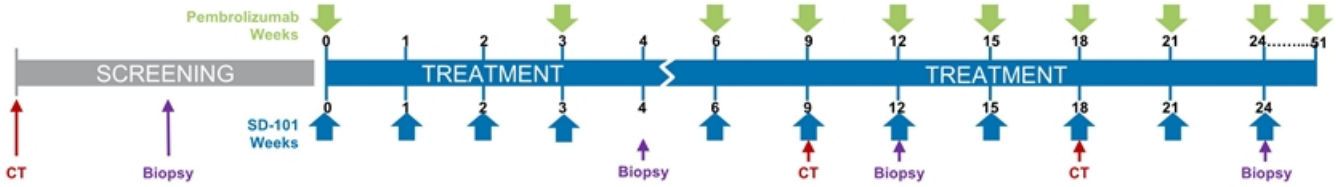
TLR agonists


Tumor
NK Cell
Tumor Killing
IFNγ
IFNα
IP-10
T Cell
T Cell Homing
Tumor Killing
IFNα
Plasmacytoid Dendritic Cell
SD-101
MyD88
TLR9
NF-kB
MHC
CD40
CD86
CD8+ T Cell
Cytokines
MyD88
TLR9
IRF-7
IFNα
IFNα
Tumor Antigens
Dying Tumor
MHC
CD40
CD86
Naïve T Cell

Methods

Phase 1b/2 Trial (SYNERGY-001/KEYNOTE-184)

- **Patients:**
  - Advanced/metastatic head and neck squamous cell carcinoma
  - Prior anti-PD-1/PD-L1 naïve
  - ECOG performance status of 0 or 1
  - At least one injectable lesion
- **Study Treatment:**
  - Two dose levels were assessed: 8 mg one lesion and 2 mg per lesion up to 4 lesions
  - Pembrolizumab was administered IV (200 mg Q3W)
- **Primary Endpoint**: Objective response rate by RECIST v1.1
- **Secondary Endpoints:** Safety and tolerability, progression-free survival, duration of response, and immunophenotype of the tumor microenvironment



 Cohen E, et al. Abstract 3560

Efficacy

Objective Response Rate

	8 mg	2 mg
mITT patients, n*	22	2
Objective response rate, n (%)	6 (27.3)	
95% confidence interval	(16, 56)	
Best overall response, n (%)		
Complete response	0	
Partial response	6 (27.3)	
Stable disease	4 (18.2)	2 (100)
Progressive disease	10 (45.5)	
Time to response (months)		
Median (min, max)	2.1 (2.0, 4.2)	
Duration of response (months)		
Median (min, max)	3.6+ (0.0, 6.9)	

* mITT: excluding patients on treatment but did not yet have their first Ct scan and tumor assessment

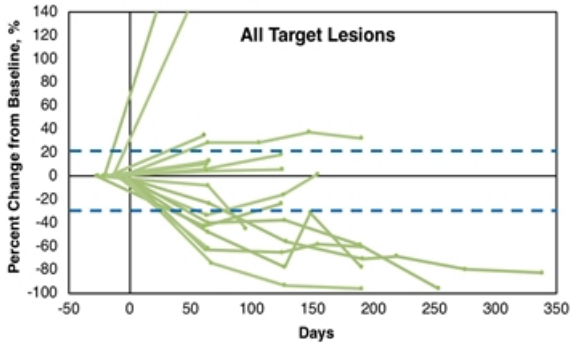
PD-L1 Expression Data and Efficacy, 8 mg

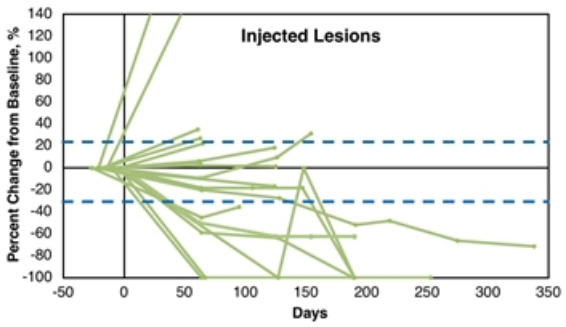
Subject	Dose (mg)	BOR	TPS	
1	8	PD	0	PD-L1 negative
2	8	PD	0	
3	8	PR	<1	PD-L1 positive
5	8	SD	2	
6	8	PD	5	
7	8	PD	10	
8	8	PD	10	
9	8	PD	15	
10	8	PR	30	
11	8	PR	40	
12	8	PD	60	
14	8	PR	90	
15	8	PD	95	

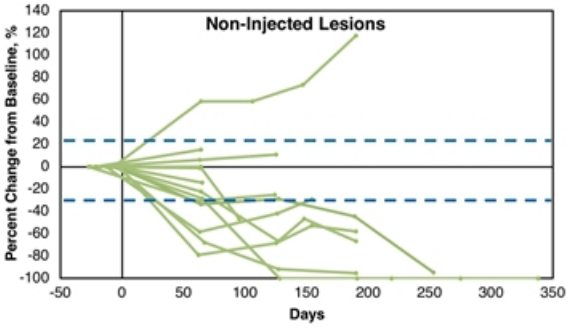
TPS: tumor proportion score; additional PD-L1 expression data pending

 Cohen E, et al. Abstract 3560

Percent Change From Baseline for Target Lesions, 8 mg







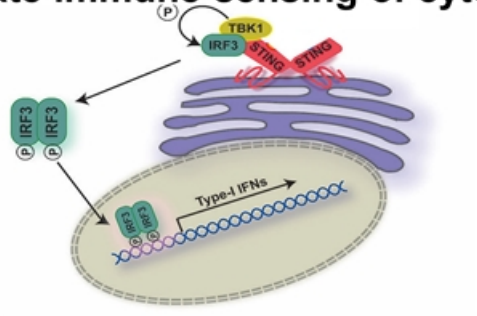
171 Cohen E, et al. Abstract 3560

UC San Diego Health

STING

STING Agonists

- **St**imulator of **In**terferon **G**enes
- Discovered from expression cloning using IFN-β reporter
- ER resident cytosolic PAMP and indirect DAMP (DNA Damage Sensor)
- Potent antiviral activity
- Required for innate immune-sensing of cytosolic DNA



STING is a central mediator in the cytosol for activating innate immunity in response to nucleic acids

ER, endoplasmic reticulum

Ishikawa H, et al. *Nature*. 2008;455(7213):674-678.

Preliminary Results of the First-in-Human Study of MK-1454, an Agonist of Stimulator of Interferon Genes (STING), as Monotherapy and in Combination With Pembrolizumab in Patients With Advanced Solid Tumors or Lymphomas

Study Design

Table 2. Dose-Limiting Toxicities

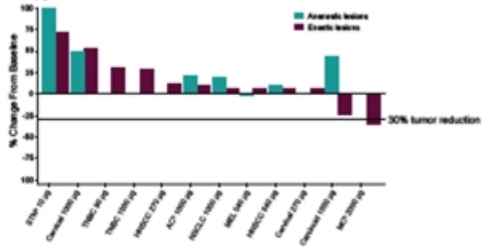
Dose Group	n/N[a]	DLT
1500 µg Arm 1 monotherapy	1/6	Vomiting Grade 3
540 µg Arm 2 combination therapy	1/9	Erythema multiforme Grade 2[b]
1500 µg Arm 2 combination therapy	2/14	Injection site pain Grade 3, skin/tumor necrosis Grade 3

Table 4. Summary of Best Overall Response With Confirmation Based on Investigator Assessment per RECIST 1.1 (FAS Population)

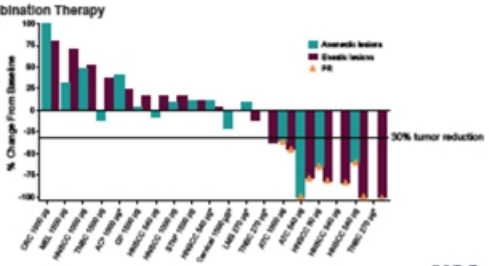
Response n (%)	Arm 1 Monotherapy Total N=20[a]	Arm 2 Combination Therapy Total N=25[a,b]
Complete response	0 (0.0)	0 (0.0)
Partial response	0 (0.0)	6 (24.0)
Stable disease	4 (20.0)	6 (24.0)
Disease control	4 (20.0)	12 (48.0)
Progressive disease	9 (45.0)	9 (36.0)
Nonevaluable[c]	1 (5.0)	0 (0.0)
No assessment[d]	6 (30.0)	4 (16.0)

Figure 3. Maximum Percentage Change From Baseline in Target Injected (Enestic) vs Non-injected (Anenestic) Lesions (Investigator Review, RECIST 1.1)

A. Monotherapy



B. Combination Therapy



UC San Diego Health

Phase Ib study of MIW815 (ADU-S100) in combination with spartalizumab (PDR001) in patients with advanced/metastatic solid tumors or lymphomas (NCT03172936)

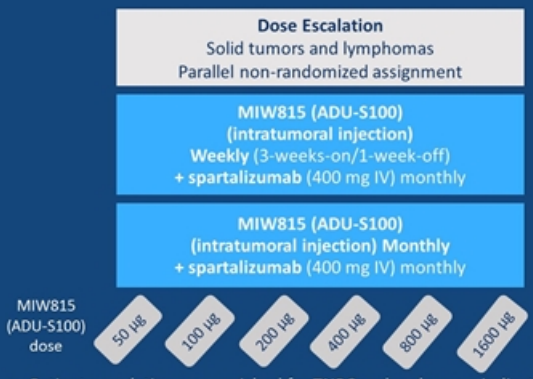
Funda Meric-Bernstam,[1] Shahneen Sandhu,[2] Omid Hamid,[3] Anna Spreafico,[4] Stefan Kasper,[5] Reinhard Dummer,[6] Toshio Shimizu,[7] Neeltje Steeghs,[8] Nancy Lewis,[9] Craig Talluto,[10] Sinead Dolan,[10] Andrew Bean,[9] Robert J. Brown,[11] Damian Trujillo,[11] Nitya Nair,[11] Jason J. Luke[12]

[1]Department of Investigational Cancer Therapeutics, MD Anderson Cancer Center, Houston, TX; [2]Peter MacCallum Cancer Centre, Melbourne, Australia; [3]The Angeles Clinic and Research Institute, Los Angeles, CA; [4]Division of Medical Oncology and Hematology, Princess Margaret Cancer Centre, Toronto, ON, Canada; [5]Department of Medical Oncology, West German Cancer Centre, University Hospital Essen, Essen, Germany; [6]University of Zurich, Zurich, Switzerland; [7]National Cancer Center Hospital, Tokyo, Japan; [8]Netherlands Cancer Institute, Amsterdam, The Netherlands; [9]Novartis Pharmaceuticals Corporation, East Hanover, NJ; [10]Novartis Institutes for BioMedical Research, Cambridge, MA; [11]Aduro Biotech Inc., Berkeley, CA; [12]The University of Chicago Medicine, Chicago, IL

PRESENTED AT: 2019 ASCO ANNUAL MEETING #ASCO19

PRESENTED BY: Dr Funda Meric-Bernstam

Ph Ib MIW815 (ADU-S100) + spartalizumab in patients with advanced solid tumors or lymphomas



Key inclusion criteria:

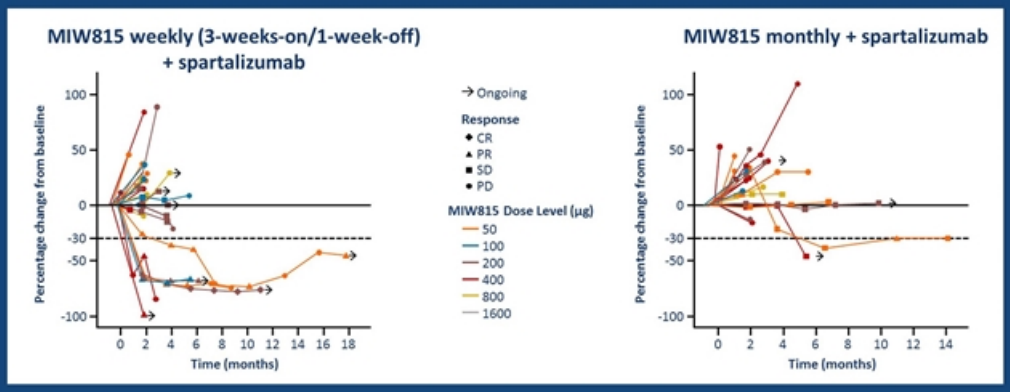
- Ability to undergo tumor biopsies of injected and non-injected lesions
  - Injectable lesions are cutaneous, subcutaneous, or nodal
- Prior immunotherapy is permitted

Data cut-off: April 5, 2019
Primary objective: Safety and tolerability
Secondary objectives: Preliminary anti-tumor activity, PK, and PD

- Patient population was enriched for TNBC and melanoma indications by allowing backfill of lower dose cohorts

NCT03172936
IV, intravenous; MTD, maximum tolerated dose; PD, pharmacodynamics; PK, pharmacokinetics, RDE, recommended dose for expansion; TNBC, triple negative breast cancer.

Percentage change from baseline
Sum of target lesion diameters (evaluable patients)



Data cut-off: April 5, 2019

Cytokines

Initial report of intratumoral tavokinogene telseplasmid with pembrolizumab in advanced melanoma: an approach designed to convert PD-1 antibody progressors into responders (NCT03132675)

Poster 717 / Abstract 11375
Society for Immunotherapy of Cancer
November 9–11, 2018; Washington, DC, USA

Victoria Atkinson[1], Andrew Haydon[2], Phillip Parente[3], Tom van Hagen[4], Gregory A. Daniels[5], Pablo Fernandez-Penas[6], Mecker Moller[7], Igor Puzanov[8], Sajeve Thomas[9], Robert H. Andtbacka[10], Clemens Krepler[11], Rachel Roberts-Thomson[12], Alain Algazi[13], Lauren Svenson[14], Erica Browning[14], David A. Canton[15], Christopher Twitty[16], Sharron E. Gargosky[16], Adil I. Daud[17]

[1]Icon Haematology Hospital, Windsorgardens, AU; [2]The Alfred Hospital, Melbourne, AU; [3]Eastern Health Monash University, Melbourne, AU; [4]St John of God Hospital, Subiaco, AU; [5]University of California San Diego, San Diego, CA, USA; [6]Westmead Hospital, Sydney, AU; [7]University of Miami, Miami, USA; [8]Roswell Park Comprehensive Cancer Center, Buffalo, NY, USA; [9]UF Health Cancer Center at Orlando Health, Orlando, USA; [10]University of Utah, Salt Lake City, USA; [11]Merck & Co., Inc., Kenilworth, NJ, USA; [12]Calvary North Adelaide Hospital, North Adelaide, AU; [13]UCSF Helen Diller Family Comprehensive Cancer Center, San Francisco, CA, USA; [14]Oncolus Medical Incorporated, San Diego, CA, USA

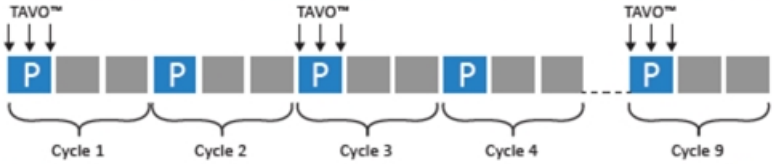
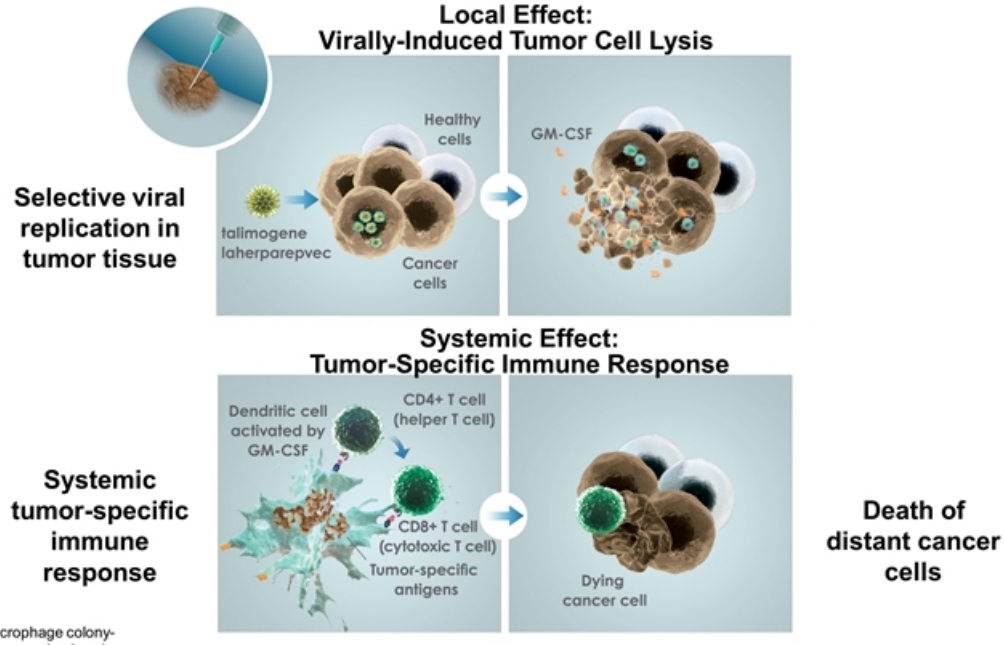


Table 2. Summary of response for the patients who completed 12 weeks of treatment

Patient number	Prior anti–PD-1 treatments (no. of cycles)	Definitive progression on prior anti–PD-1 treatment	Population who reached initial tumor assessment (~12–15 weeks) post-completion of 2 cycles of TAVO™ (N = 9)
1	Pembrolizumab IV (7)	YES	PR
2	Adjuvant pembrolizumab IV (9) Nivolumab IV (4) Nivolumab IV (4)	YES	PR
3	Pembrolizumab IV (10)	YES	SD
4	Pembrolizumab IV (4)	YES	iUPD; iSD (SD TL / new NTL)
5	Nivolumab IV (8) Pembrolizumab IV (4) Nivolumab IV (4) Nivolumab IV (once)	YES	iUPD; WDC (PR TL / new NTL)
6	Pembrolizumab IV (18)	YES	iUPD; WDC (SD TL / new NTL)
7	Pembrolizumab IV (4)	YES	PD
8	Pembrolizumab IV (11) Nivolumab IV (16)	YES	PD
9	Pembrolizumab IV (7)	YES	PD

Oncolytic Viruses

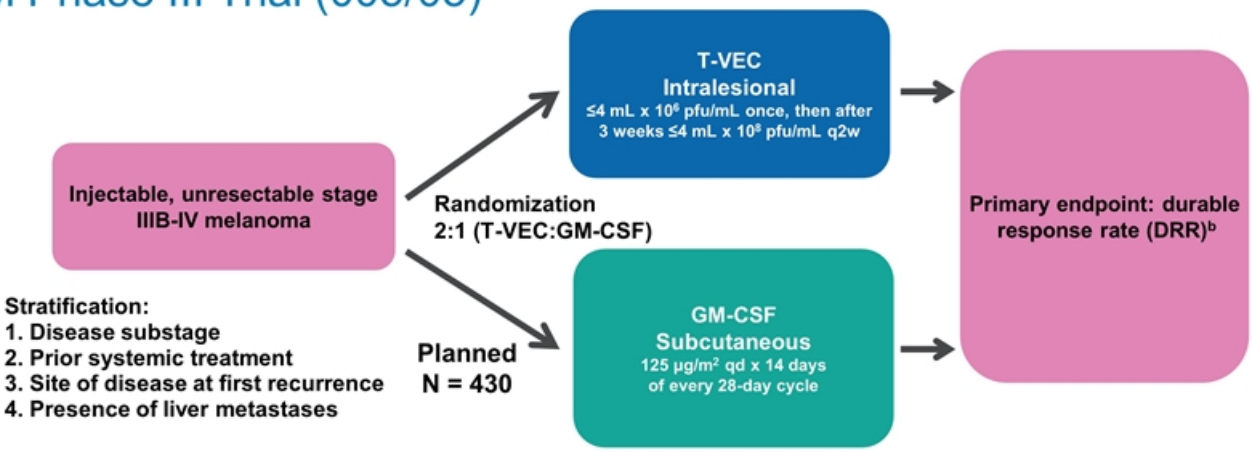
T-VEC: An HSV-1–Derived Oncolytic Immunotherapy Designed to Produce Local and Systemic Effects



GM-CSF, granulocyte-macrophage colony-stimulating factor; HSV, herpes simplex virus

Kaufman HL, et al. *J Clin Oncol*. 2014;32(Suppl): Abstract 9008a.

OPTiM Phase III Trial (005/05)



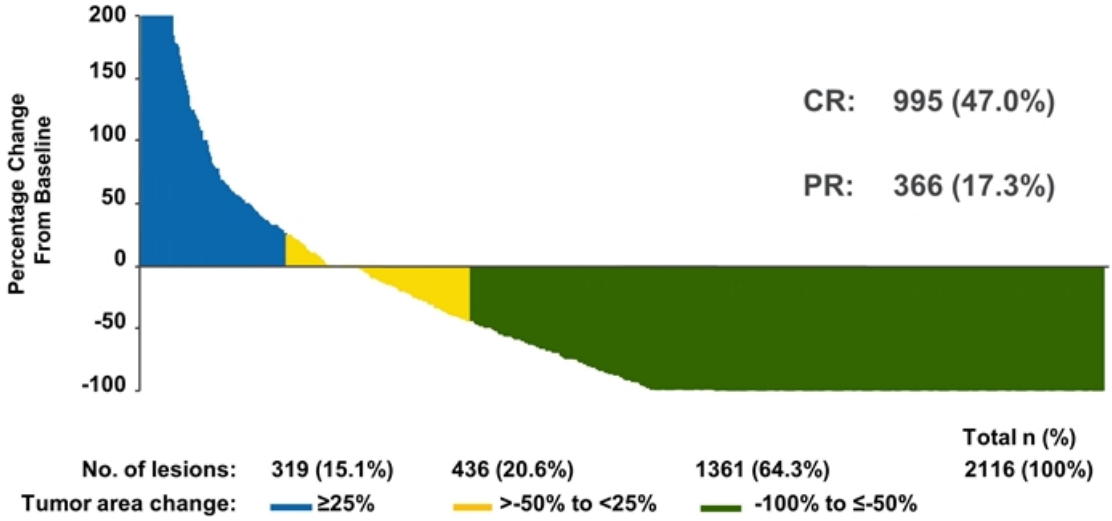
Primary endpoint: DRR: rate of CR or PR that began at any point within 12 months of initiation of therapy and lasted continuously for 6 months or longer[a]

Secondary endpoints: Overall survival (OS), objective overall response rate (ORR; CR + PR), safety

[a]Determined using modified WHO criteria by an independent, blinded endpoint assessment committee. [b]Patients were to remain on treatment for at least 24 weeks despite progression (unless intolerable adverse events [AEs] or investigator decision to start new therapy)

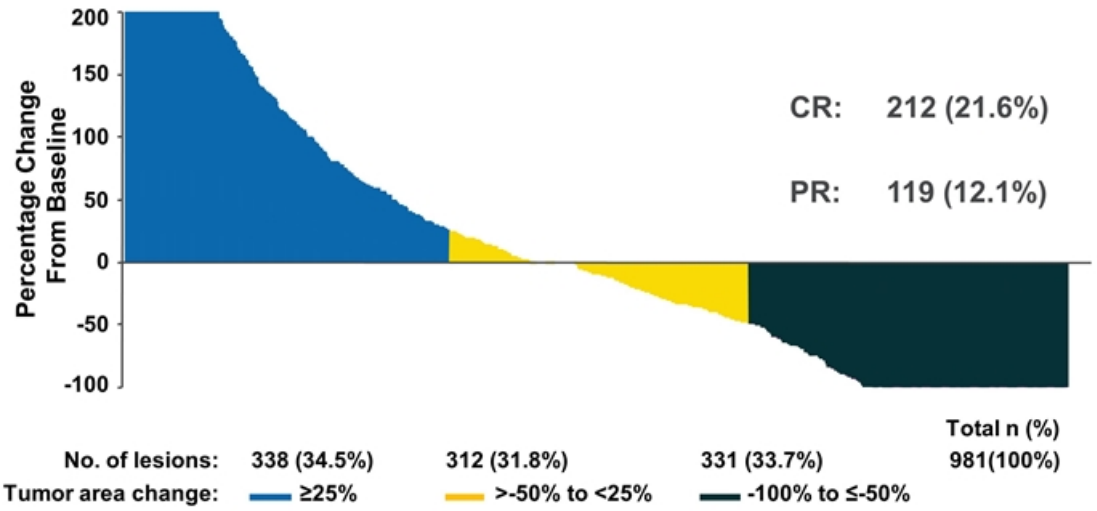
 Andtbacka RHI, et al. *Ann Surg Oncol.* 2014;21(Suppl 1): Abstract 52. Andtbacka RHI, et al. *J Clin Oncol.* 2015;33(25):2780-2788.

64% of Injected Lesions Responded to T-VEC



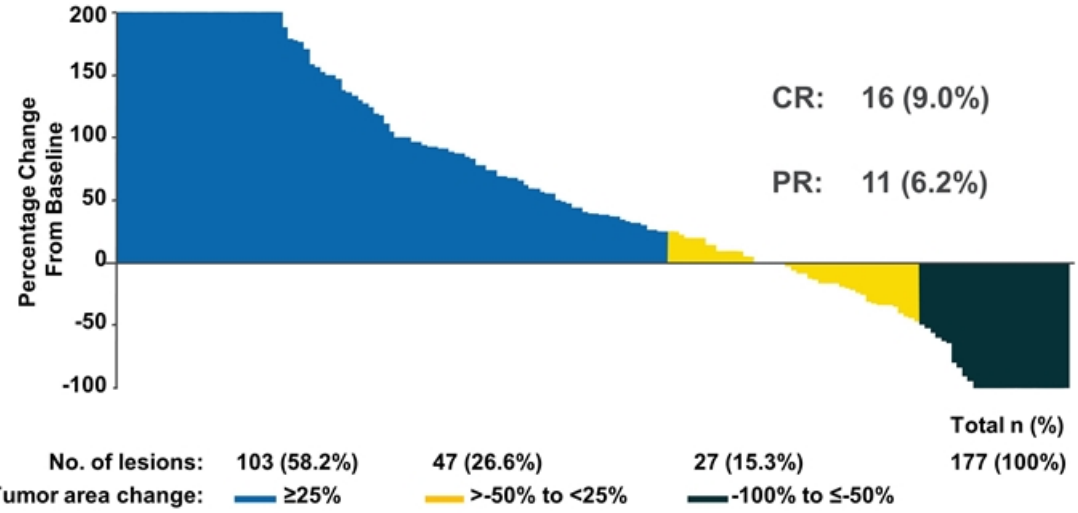
183 Andtbacka RH, et al. *Ann Surg Oncol*. 2014;21(Suppl 1): Abstract 52.

34% of Noninjected, Nonvisceral Lesions Responded to T-VEC



184 Andtbacka RH, et al. *Ann Surg Oncol*. 2014;21(Suppl 1): Abstract 52.

15% of Visceral Lesions Responded to T-VEC

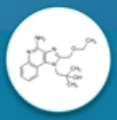


185 Andtbacka RH, et al. *Ann Surg Oncol*. 2014;21(Suppl 1): Abstract 52.

Conclusions

- Preclinical and clinical evidence supports induction of immune tumor infiltration and necrosis with multiple intratumoral approaches (oncolytic virus, TLR agonist, etc)
- Mechanism of action and clinical responses in noninjected tumors indicate that there is a systemic antitumor effect
- New treatment paradigms and technologies are needed to further improve efficacies and expand patient populations who benefit

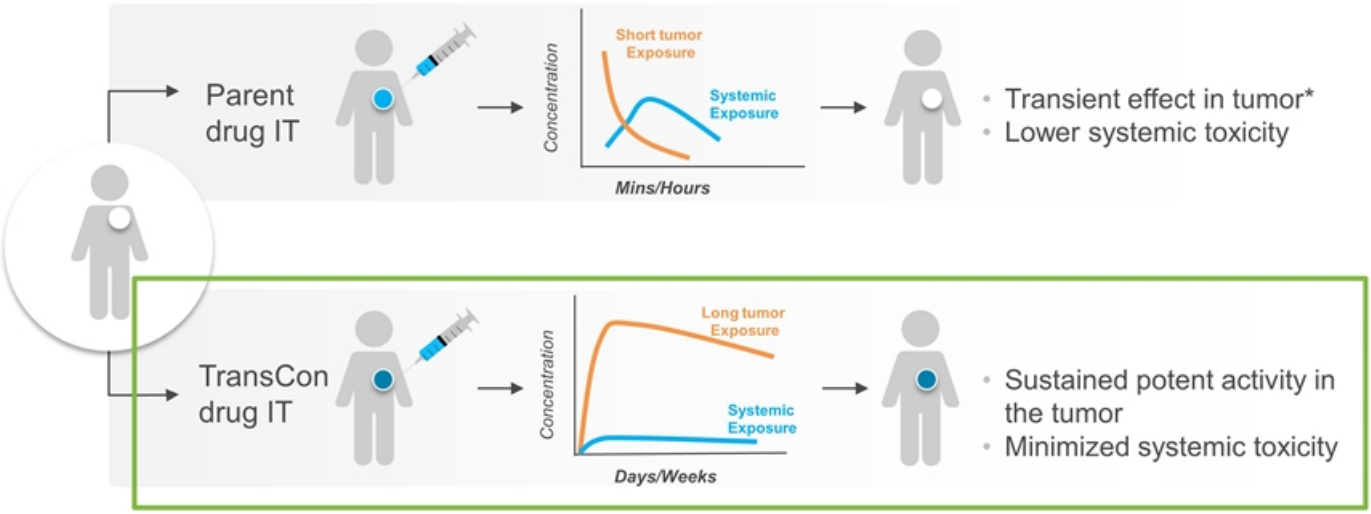
Product Candidates in Oncology



TransCon TLR 7/8 Agonist

Potential to Transform Efficacy, Safety and Practicality of Intratumoral Treatments

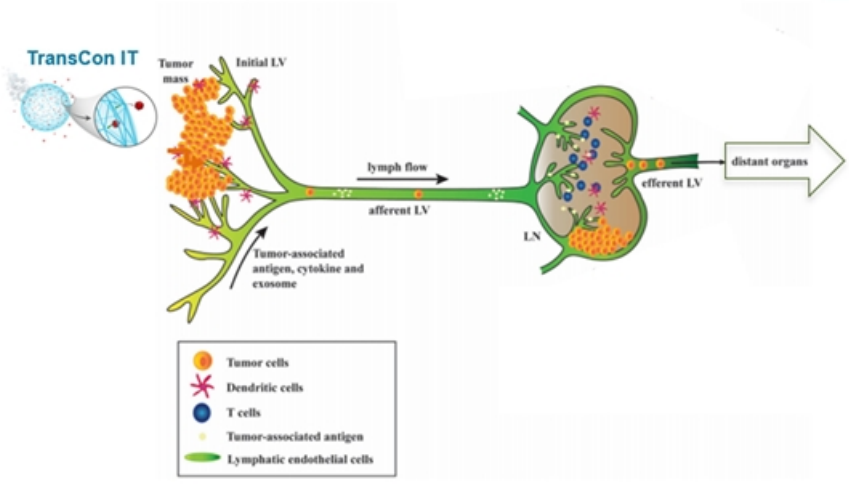
TransCon expected to provide weeks of drug exposure in the tumor, with minimal systemic toxicity



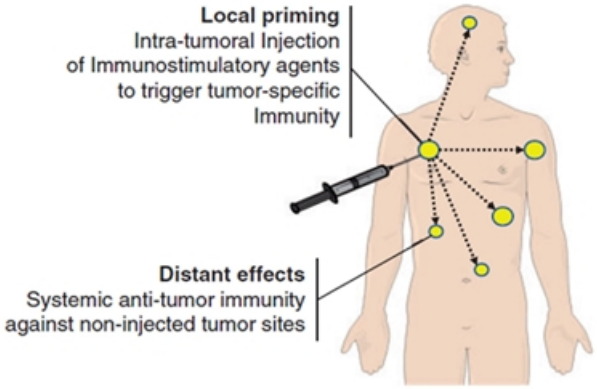
* Example: STING agonist "plasma half-life ranging from 8 to 28 min" (Meric-Bernstam, ASCO, 2019)

TransCon IT Designed for Systemic Anti-tumor Effects

Designed to Enable Immune Priming in the Draining Lymph Nodes



Cytotoxic T effector Cells Primed in Lymph Nodes Migrate to Distant Organs to Target Metastatic Cells



Adapted from Yeo et al, Front. Immunol., 2017; and Marabelle et al., Ann Onc, 2017

ascendis pharma

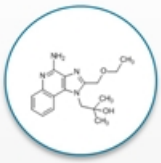
Opportunity for TransCon TLR 7/8 Agonist

Efficacy
- Sustained exposure is needed to enhance activation in the tumor
- Reduce risk of reaching super-high “ablative” levels

Safety
- Systemic toxicity dose-limiting with current approaches tolerated
- Infrequent dosing expected to improve practicality and reduce injection-related complications

New Indications
- Patients on poorly tolerated combos
- Hard-to-inject tumors that cannot be injected frequently enough with alternative approaches

TransCon TLR 7/8 Agonist



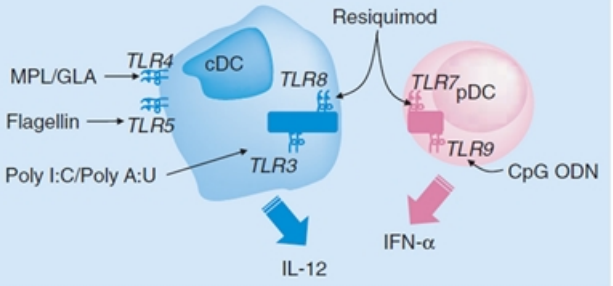
Designed for tumor-localized, sustained release with ***minimal systemic exposure*** aiming for ***superior efficacy***

TLRs: Innate Immune Sensors of “Danger” Associated with Pathogens or Cell Death

Toll-like receptors:

- Receptors for Pathogen- or Danger- (cell death) Associated Molecular Patterns
- Elevate proinflammatory cytokines: IL-12, IFNs, TNF-a, IL-1, chemokines
- Enhance antigen presentation: upregulated MHCII, costimulatory molecules (e.g. CD80/86)

Resiquimod Activates both Conventional Dendritic Cells (DC) and Plasmacytoid DCs



Adapted from Vasilakos & Tomai, Exp Rev Vaccines, 2013

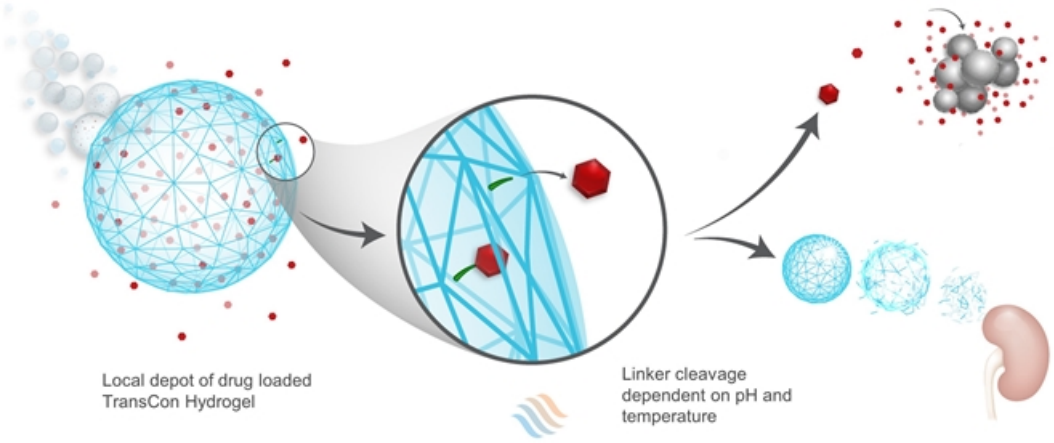
TLRs activate several key pathways critical in host defense against tumors

Clinical Validation on Several TLR Agonists and IT Treatments

- Intravesical BCG bacilli (TLR 2 and 4 agonist) approved for superficial bladder cancer
- Topical TLR 7 agonist, imiquimod, approved for basal cell carcinoma
- TLR 7/8 agonist, resiquimod, demonstrated efficacy in cutaneous T cell lymphoma
- Intratumoral T-VEC, talimogene laherparepvec, approved in advanced melanoma
- Several ongoing clinical trials with TLR agonists in combination with checkpoint blockade and/or cytokines

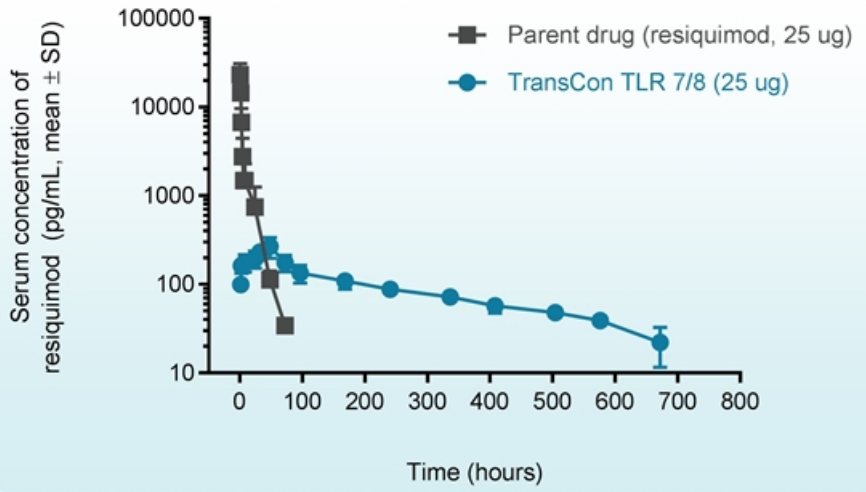
References: Prescribing Information for TICE® BCG, Aldara®, Imlygic®; Rook et al., Blood 2015 126:1452-1461

Resiquimod Loaded onto TransCon Hydrogel for Intratumoral Sustained Delivery



- Resiquimod transiently conjugated to TransCon Hydrogel carrier, designed to provide sustained local release of unmodified parent drug
- Designed to provide sustained activation of tumoral myeloid lineages driving tumor antigen release/presentation and induction of immune stimulatory cytokines

Sustained Release of Resiquimod over 4 Weeks in Rats Following *Subcutaneous* Administration



Parent Drug:
$T_{1/2}$ = ~10 h

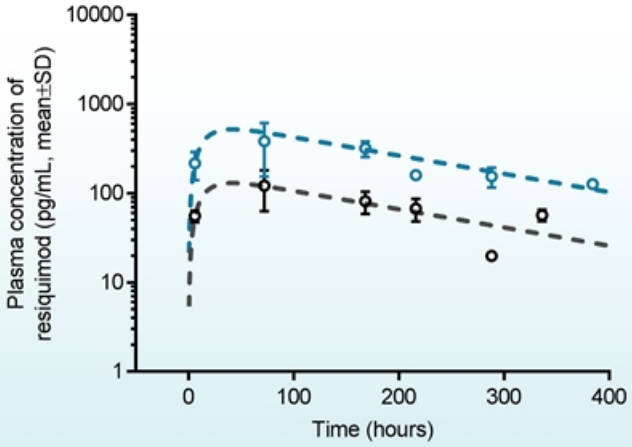
TransCon TLR 7/8:
$T_{1/2}$ = ~250 h

- Subcutaneous injection of 25 ug (resiquimod equivalent, ~0.075 mg/kg) in Wistar Rats

TransCon technology enables 25-fold increased half-life and avoids high Cmax

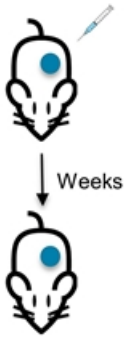
ascendis pharma

Sustained Release of Resiquimod for Weeks Following *Intratumoral* Administration in Mice



TransCon TLR 7/8 IT:
$T_{1/2}$ = ~280 hours
(~12 Days)

IT injection of TransCon TLR 7/8 Agonist

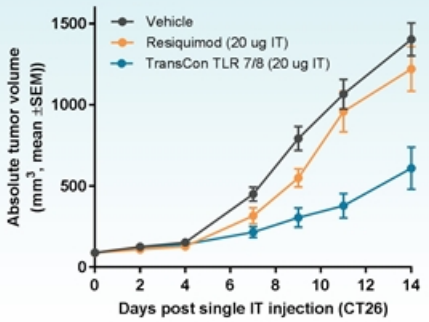


- A single 5 or 20 ug IT dose into CT26 tumors (~0.25 mg/kg or 1 mg/kg)
- The plasma concentration-time profiles were modeled simultaneously with a unified set of parameters

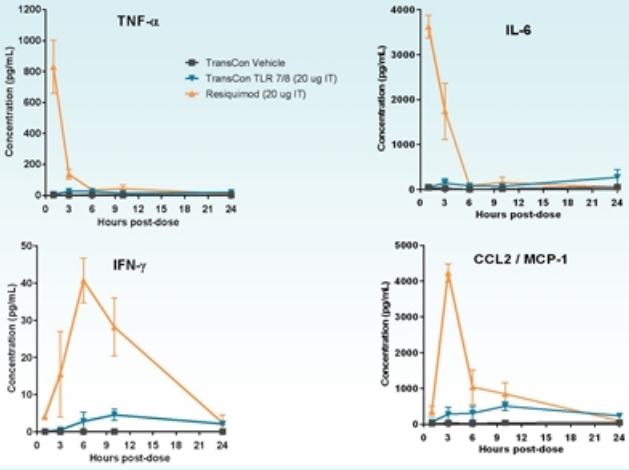
ascendis pharma

Single Dose of TransCon TLR 7/8 Agonist Provided Potent Tumor-growth Inhibition with Minimal Increase in Cytokines

More Potent Tumor Growth Inhibition by TransCon TLR7/8 than Comparable Dose of Resiquimod



Lower Systemic Cytokine Release by TransCon TLR 7/8 than Comparable Dose of Resiquimod



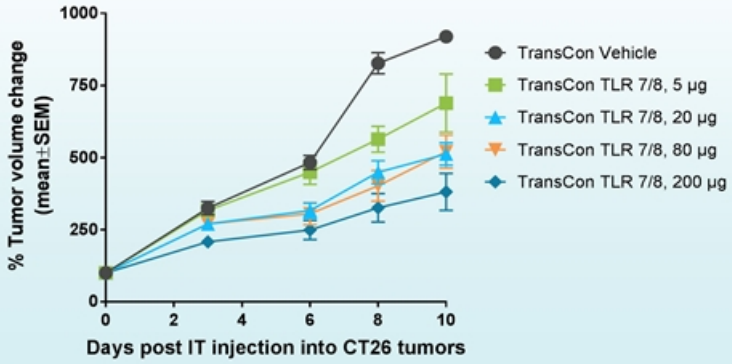
TransCon TLR 7/8 Agonist has the potential to provide more potent anti-tumor benefits without dose-limiting toxicity, as IL-6 and TNF-α associate with cytokine release syndrome and sepsis in patients

Gullo et al., Front Biosci, 2010; Norelli et al., Nat Med, 2018

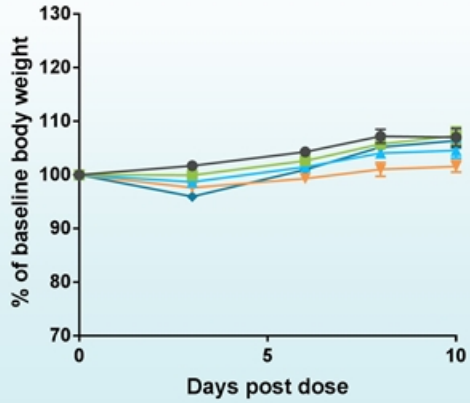
Dose-dependent Tumor Growth Inhibition Following a Single IT Injection of TransCon TLR 7/8 Agonist

Single IT Dosing

Tumor Growth: Dose-dependent Inhibition



Body Weights: All Doses Well Tolerated

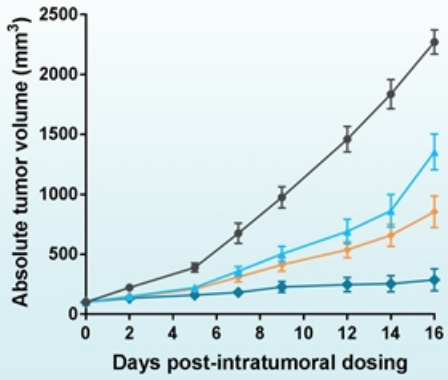


Consistent with MOA, local inflammation and some tumor ulcerations observed

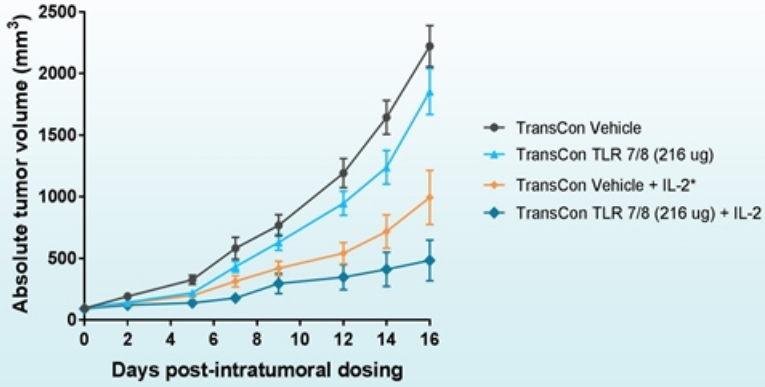
Single-dose of TransCon TLR7/8 Agonist Triggered Abscopal Anti-Tumor Inhibition and Enhanced Anti-tumor Effects of IL-2

Single IT Dosing

Injected Tumor



Non-injected Tumor



*IL-2 dosed at 20 ug twice daily on days 0-4, once daily on days 8-12

TransCon TLR 7/8 Agonist - Summary

- Offers a new treatment paradigm for intratumoral sustained delivery with potential for superior efficacy and safety
  - Single intratumoral dose potentially provides exposure for weeks/months
  - Dramatically altered ratio of anti-tumor vs systemic effects when compared to equimolar dose of parent drug
  - Potent anti-tumor effects, including abscopal effect, observed with a single dose as a monotherapy and in combinations
  - Potential to enable efficacy with dosing interval of months


Product Candidates
in Oncology
TransCon
VEGF-TKI

Opportunity for TransCon VEGF-TKI

Efficacy
- Better tolerated approaches are needed to enable sufficient tumor exposure and new combination approaches

Safety
- Lower systemic exposure expected to enable aggressive multiagent therapies

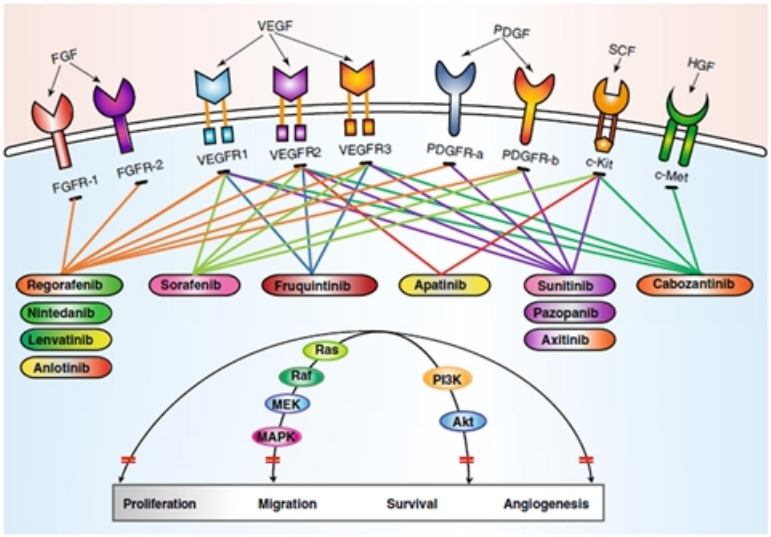
New Indications
- Patients on poorly tolerated combos
- Enable intratumoral mechanisms not achievable via oral route
- CNS tumors

TransCon VEGF-TKI

Tumor-localized, sustained release aiming for mechanisms and efficacy not achievable by oral alternatives

ascendis pharma

VEGF-TKI: Validated Drugs Offering More than Just Inhibition of Angiogenesis



Adapted from Qin et al. J Hem Oncology, 2019

- *Validated drugs* - approvals in renal cell carcinoma, thyroid cancer, hepatocellular carcinoma
  - Proven combination benefits with checkpoint blockade
- Potent, direct anti-proliferative effects on tumor cells
  - As a monotherapy at high doses (uM), at lower doses (nM) when combined with chemotherapy
- Immunomodulatory effects: improved influx and activation of immune cells, inhibition of immunosuppressive macrophages in tumors

Reference: Morelli et al., Oncotarget, 2017, Vol. 8, (No. 2), pp: 3380-3395; de Aguiar et al., Front Immunol, 2019

VEGF-TKI: TransCon Has the Potential to Achieve Tumor Levels and Activity Not Feasible by Oral Route

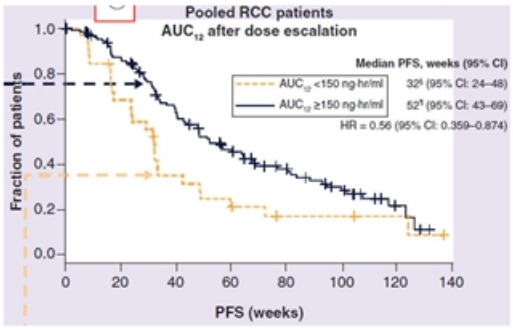
Oral VEGF-TKI not well tolerated, limiting efficacy

- Frequent dose reductions and treatment discontinuations up to ~30%
- Higher dose and exposure correlates with better outcome

Some indications poorly addressed with current drugs

- E.g. glioblastoma: bevacizumab is approved, while brain permeability of all VEGF inhibitors is limited

Higher Exposure of Axitinib Correlates with Better Outcome in Renal Cell Carcinoma

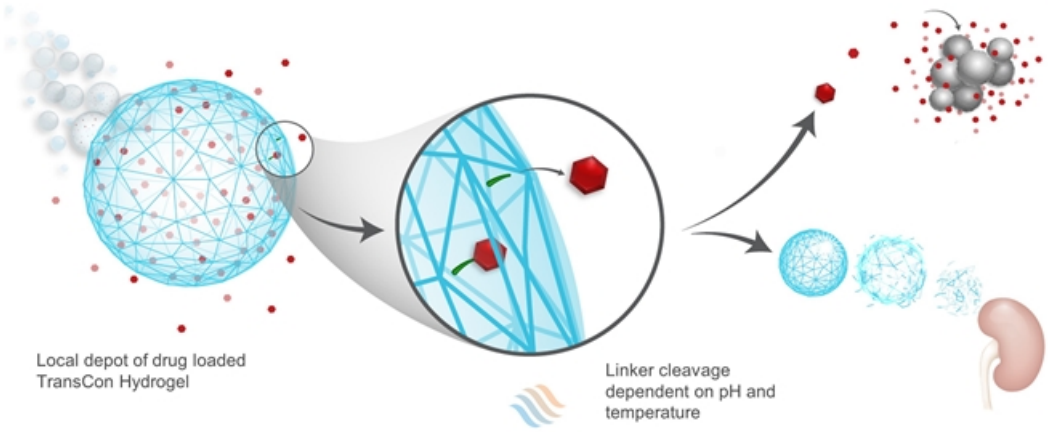


*Schmidinger et al., **Future Oncol. 14, 861,** 2018*

Expected to enable IT mechanisms not achievable via oral route: direct anti-tumor effects and modulation of tumor microenvironments

- For example, rationale to combine VEGF-TKI with PD(L)1+chemo exists, while only TransCon may enable the combination with high enough IT concentrations and acceptable toxicity

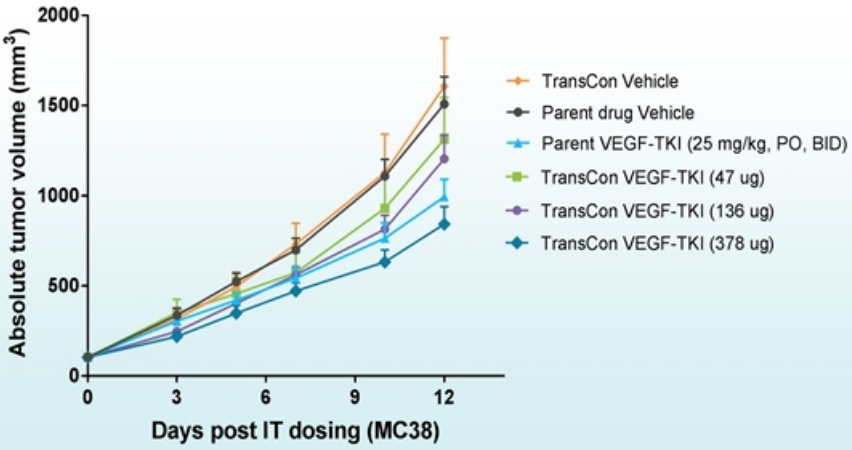
VEGF-TKI Loaded onto TransCon Hydrogel for Intratumoral Sustained Delivery



- VEGF-TKI transiently conjugated to TransCon Hydrogel carrier, designed to provide sustained release of unmodified parent drug
- Designed to provide sustained modulation of the tumor microenvironment with potential for direct anti-tumor effects

Dose-dependent Tumor Growth Inhibition by a Single Dose of TransCon VEGF-TKI

Single IT Dosing



- TransCon VEGF-TKI estimated to allow for tumor concentrations >100-fold higher than in serum
- Limited systemic exposure expected to reduce drug-related adverse events

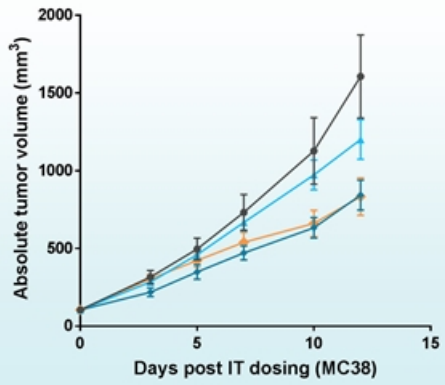
Single-dose TransCon VEGF-TKI provided at least comparable tumor growth inhibition when compared to twice daily oral dose

ascendis pharma

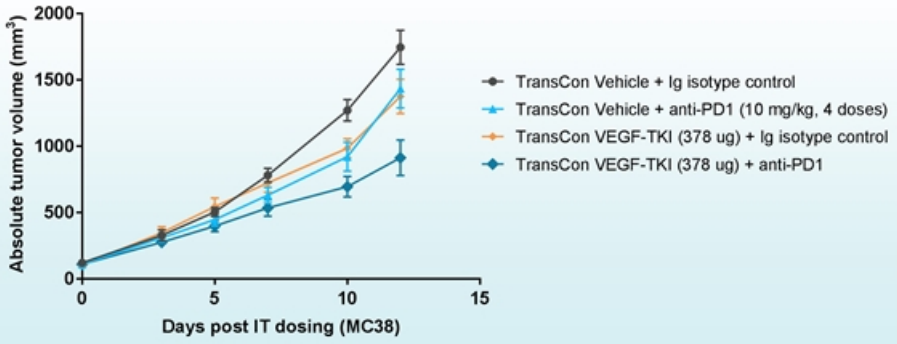
Single Dose of TransCon VEGF-TKI Allowed for Combination Benefits with anti-PD-1 Ab in Abscopal Tumor

Single IT Dosing

Injected Tumor



Non-injected Tumor



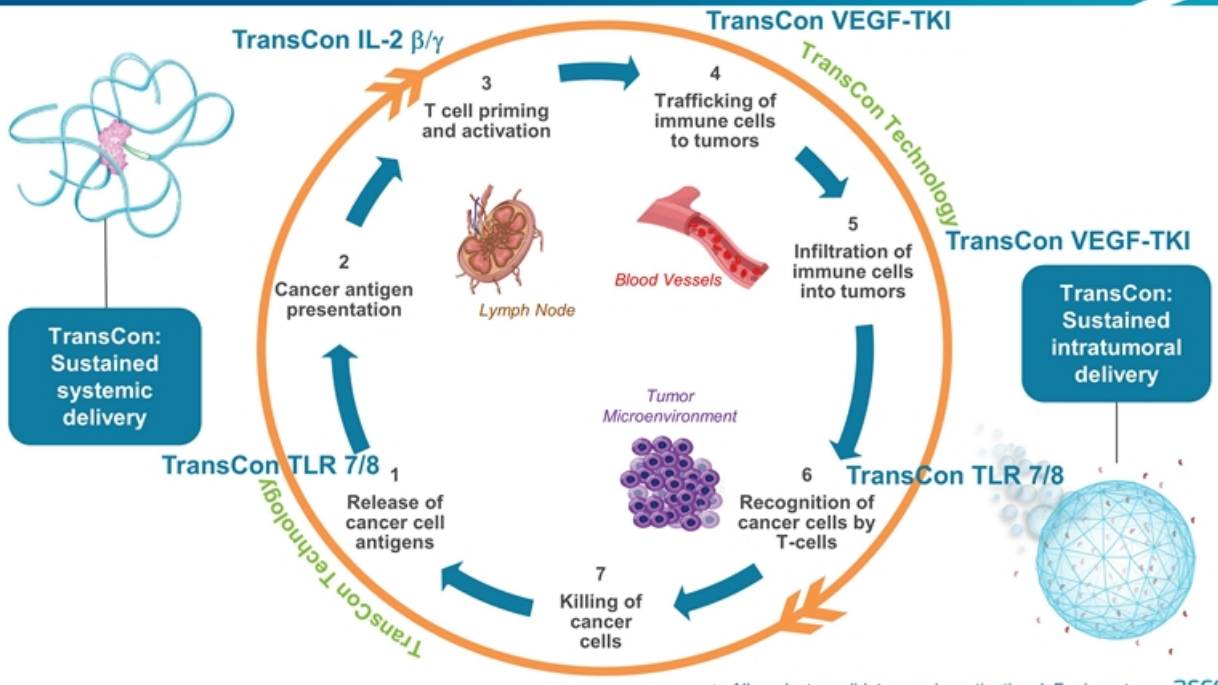
Potent Anti-Tumor Effects in Injected and Non-injected Tumors, Including Combination Benefit with Checkpoint Blockade

ascendis pharma

TransCon VEGF-TKI – Summary

- New approach to modulation of tumor microenvironments, with the potential for direct anti-tumor effects
  - TransCon Hydrogels generated for sustained release of VEGF-TKI
  - Potent anti-tumor effects in mice observed, including combination benefits with checkpoint blockade
  - Slow intratumoral release expected to enable mechanisms not achievable by oral administration
  - Potential to enable combinations with aggressive therapeutic regimens in multiple indications, including CNS tumors

TransCon Immunity Cycle: Seeking a Broad Impact



ascendis pharma

Oncology Summary

- Best-in-class potential using systemic and intratumoral TransCon technologies
- Three differentiated product candidates with potential in multiple indications
  - TransCon IL-2 β/γ
  - TransCon TLR 7/8 Agonist
  - TransCon VEGF-TKI
- Potent anti-tumor effects of TransCon oncology candidates demonstrated in preclinical studies, reflecting expected exposure profile
  - Combination benefits with cytokines and checkpoint blockade in mice
  - Desired pharmacodynamic effects in cynomolgus monkeys
- First oncology IND (or equivalent) to be filed in 2020
- Significant patent portfolio of >20 patents and applications in support of TransCon oncology candidates

TransCon: Designed for the Next Revolution in Oncology

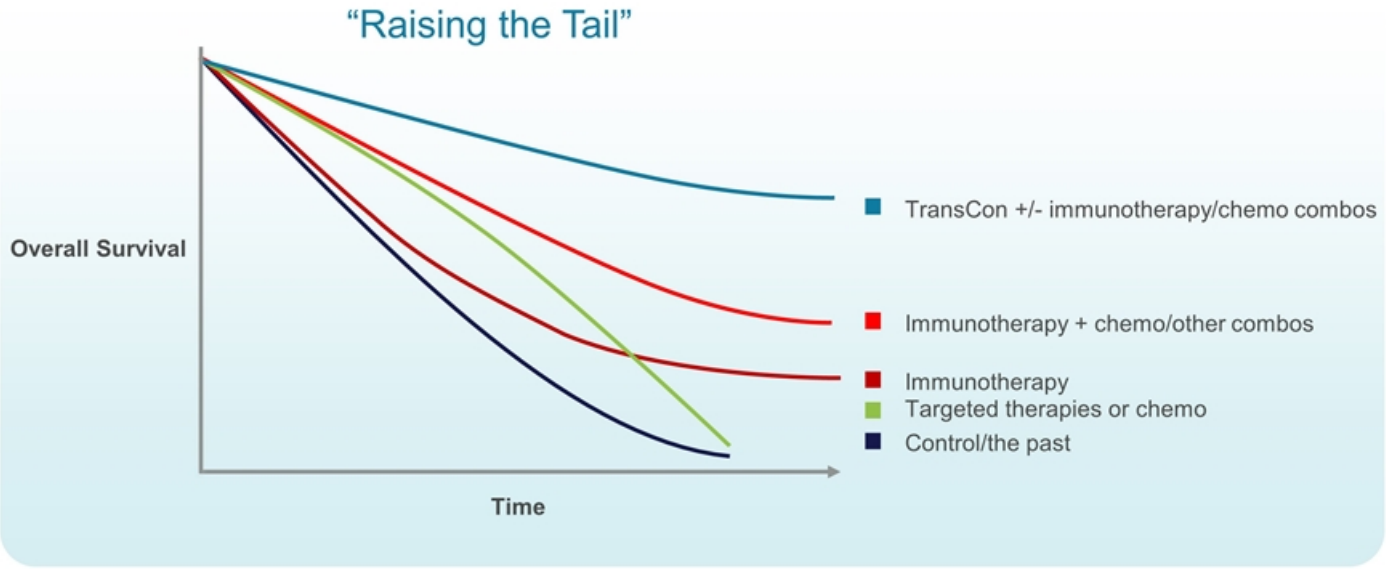
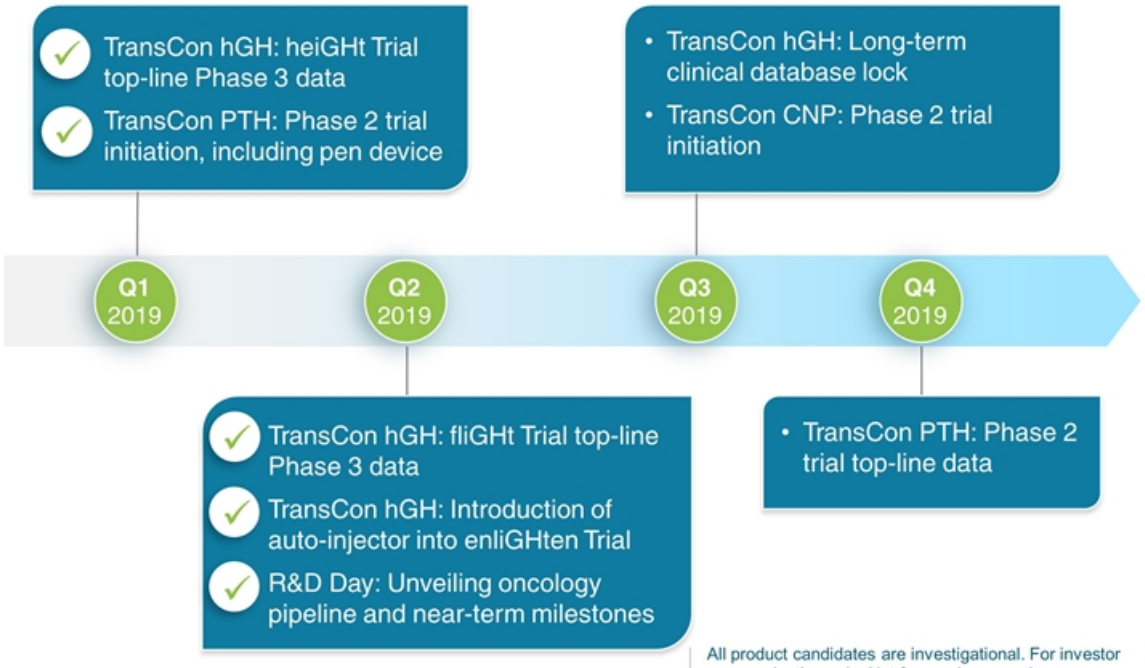


Illustration of the goal of future clinical trials involving TransCon candidates


Q & A

2019 Progress: Expected Milestones



ascendis pharma

Vision 3x3: Building a Leading BioPharma Company

Our Goal is to Achieve Sustainable Growth through Multiple Approaches

- Obtain regulatory approval for 3 Endocrinology Rare Disease products
  - TransCon hGH for pediatric growth hormone deficiency
  - TransCon PTH for adult hypoparathyroidism
  - TransCon CNP for achondroplasia
- Growth of Endocrinology Rare Disease pipeline through:
  - Label expansion programs with the goal of obtaining 9 indications in total
  - Global clinical reach directly or through partnerships
- Build an integrated commercial business for our Endocrinology Rare Disease franchise in North America and select European countries
  - Establish global commercial presence with partners outside our geographic areas
- Create 3 independent therapeutic areas each with a diversified pipeline built on TransCon technologies and our unique algorithm for product innovation
  - Established oncology as next independent therapeutic area

ascendis pharma