Ascendis Pharma A/S

August 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.

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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.

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

Company Overview

- Create best in class products addressing unmet medical needs by applying TransCon™ technologies to parent drugs with clinical proof-of-concept
  - Unique algorithm for product innovation has resulted in clinical validation of 3 out of 3 product candidates within the endocrinology rare disease area
- Endocrinology rare disease internal pipeline and expected near-term milestones
  - TransCon hGH for pediatric GH deficiency: Phase 3 demonstrated superiority of TransCon hGH; BLA planned for H1 2020
  - TransCon PTH for hypoparathyroidism: Phase 2 top-line data Q4 2019
  - TransCon CNP for achondroplasia: Phase 2 initiated
- Oncology pipeline in development with highly differentiated product candidates
  - First IND filing expected in 2020
- Build leading positions for each endocrinology rare disease product with commercial focus on maximizing global reach
  - Partnership with VISEN Pharmaceuticals for commercialization of endocrinology rare disease products in China
- Established high-value collaborations with Roche/Genentech in ophthalmology and Sanofi in diabetes
- As of March 31, 2019, cash and cash equivalents of ~€696.7 million

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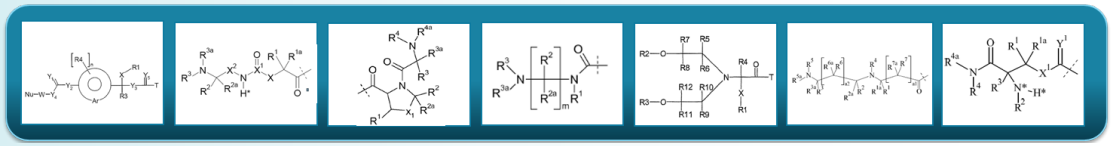
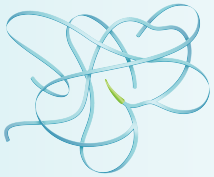
*Trans*ient *Con*jugation: Flexible and Versatile Platform

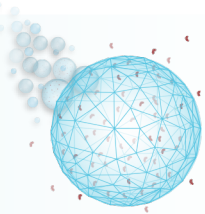
TransCon Prodrug: 3 components

- TransCon Linker
- TransCon Carrier
- Parent Drug





Soluble Carriers



Insoluble Carriers

Antibodies, Antibody Fragments, Proteins, Peptides and Small Molecules

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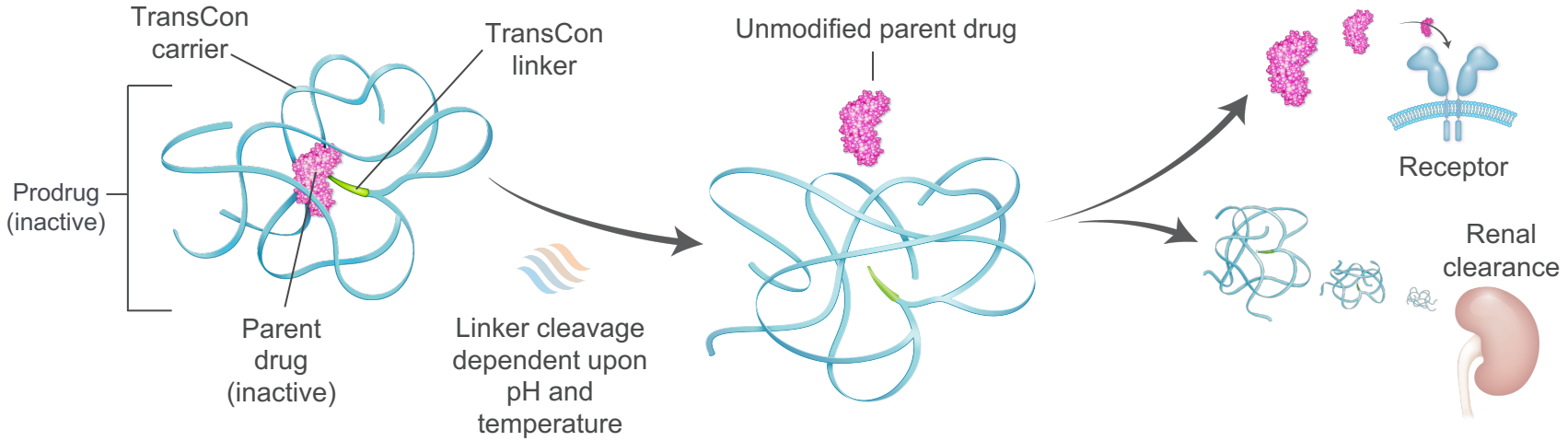
TransCon Technology: Sustained Systemic Delivery



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

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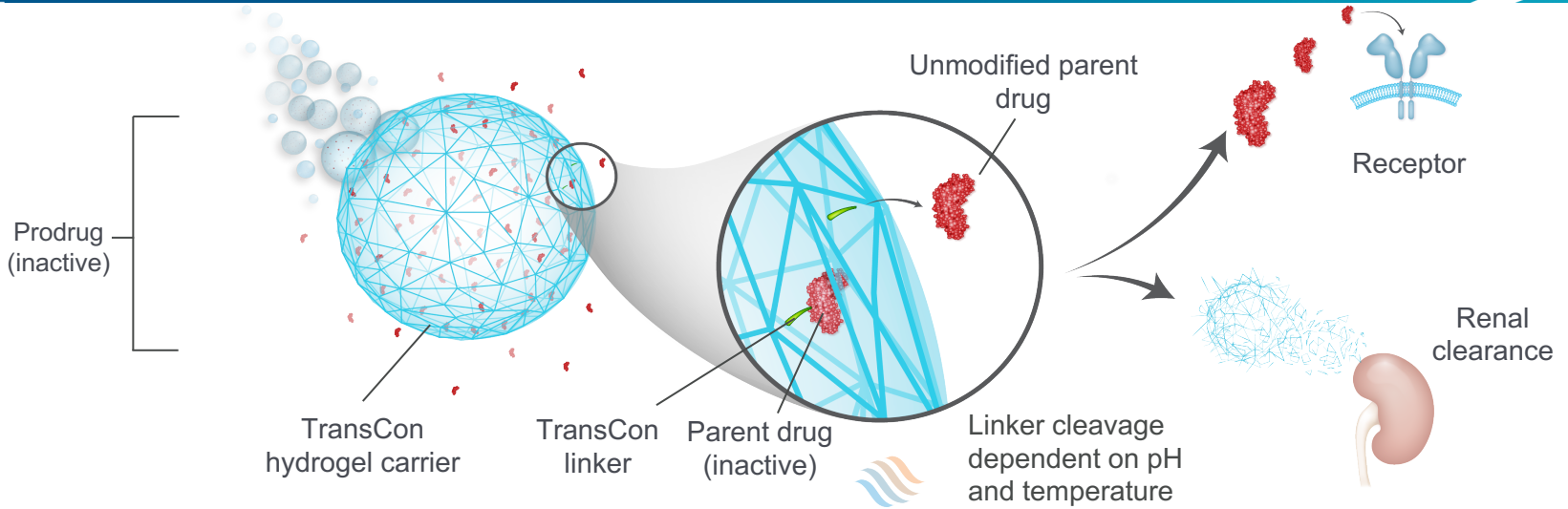
TransCon Technology: Sustained Localized Delivery

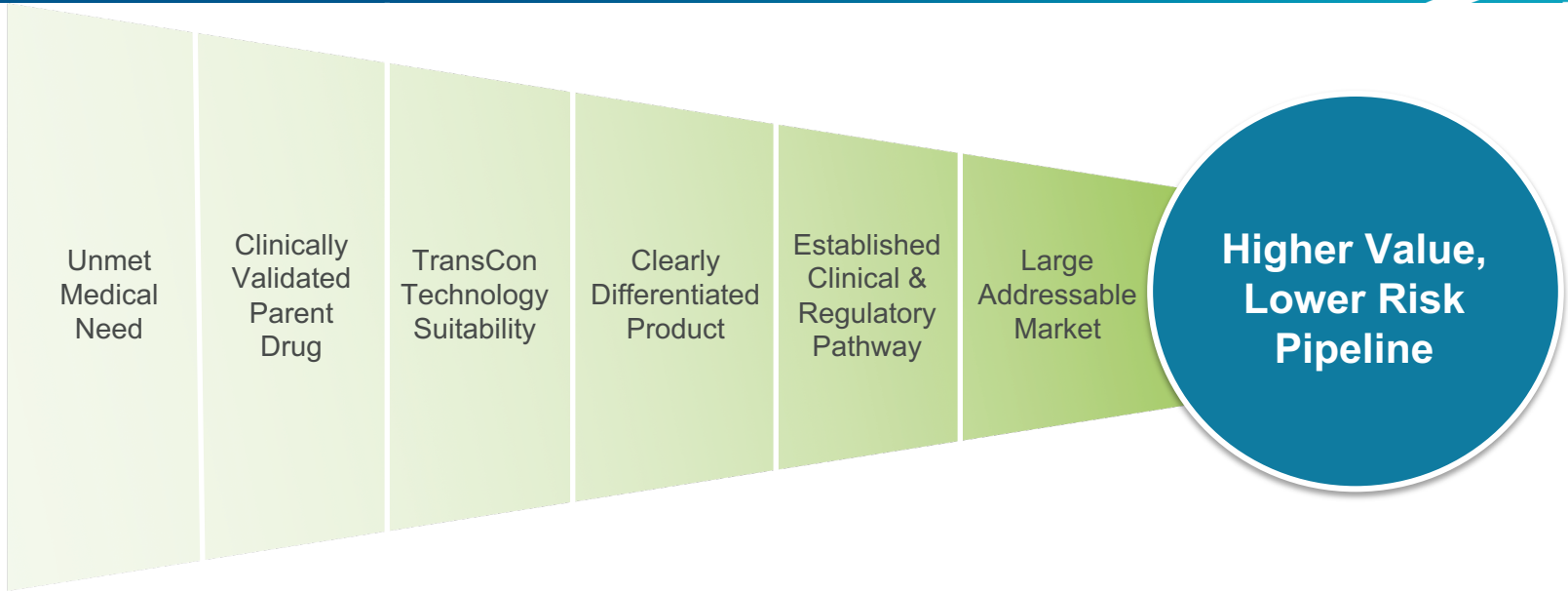


Parent drug is transiently bound to TransCon linker-hydrogel carrier, which inactivates, shields parent drug and prevents clearance

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

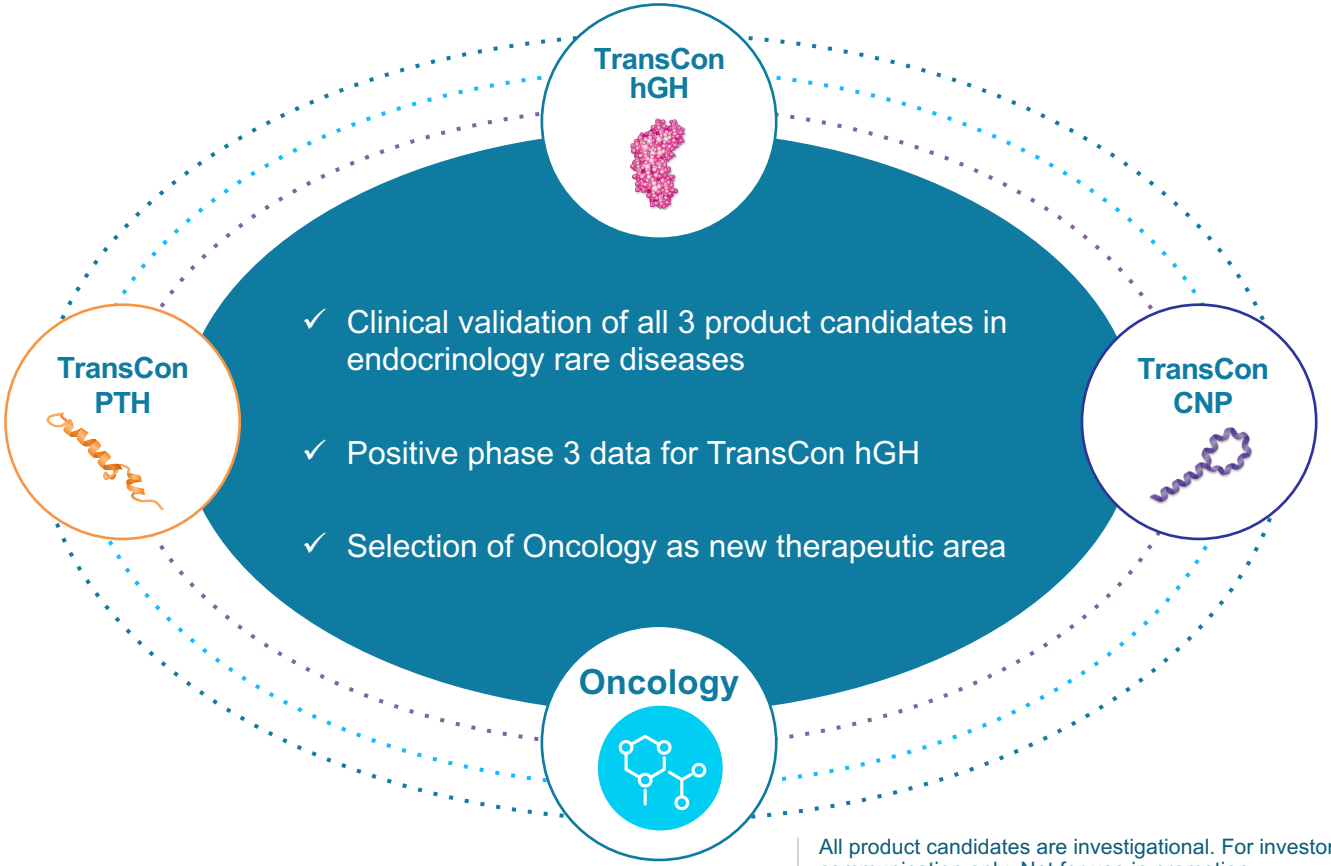
Ascendis Algorithm for Product Innovation



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

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

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TransCon™ Growth Hormone: Once-Weekly Replacement Therapy

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

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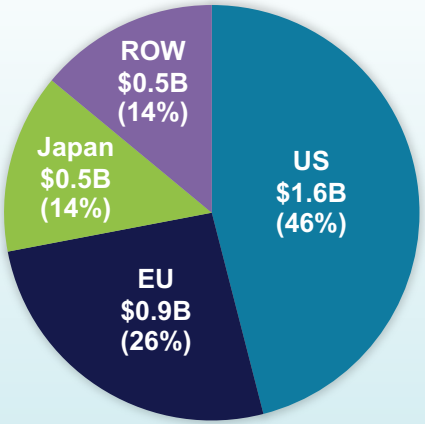
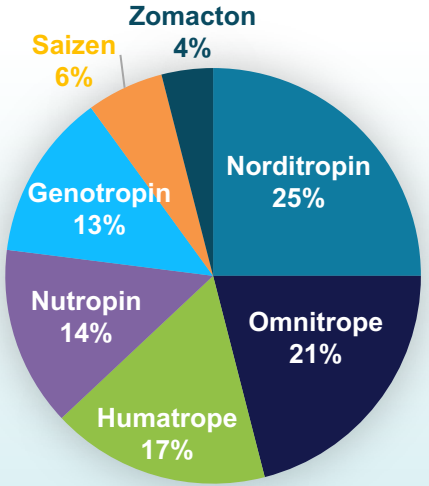
The Growth Hormone Market: Ripe for Disruption

- 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.

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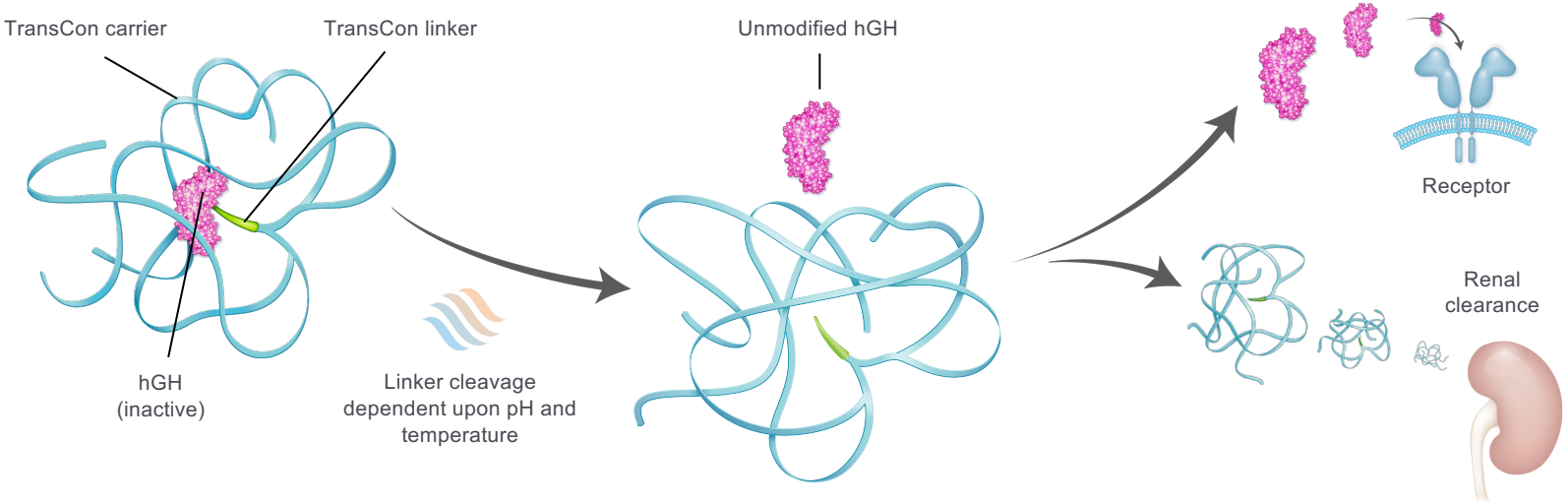
TransCon hGH Design



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

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

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)

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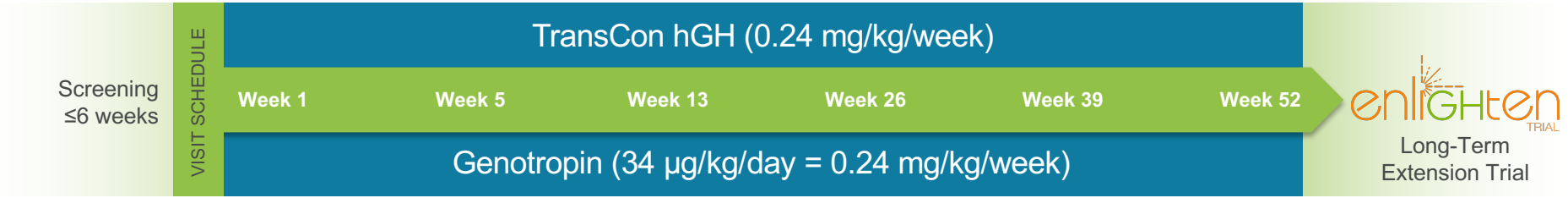
Phase 3 heiGHt Trial

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

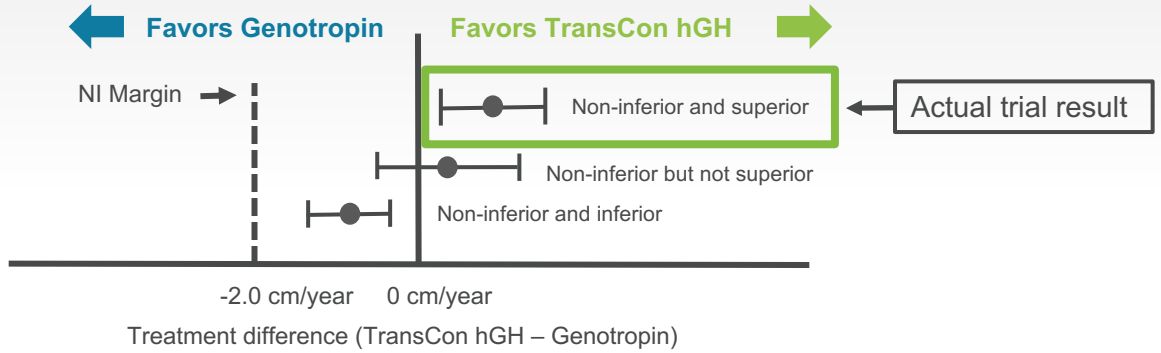
- Annualized height velocity (HV) at 52 weeks (primary endpoint)
- Annualized HV at earlier time points
- Change in height SDS over 52 weeks
- Change in serum IGF-1/IGFBP-3 levels
- Change in IGF-1 SDS and IGFBP-3 SDS
- Normalization of IGF-1 SDS
- hGH and IGF-1 levels over 168 hours at Week 13 (PK/PD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

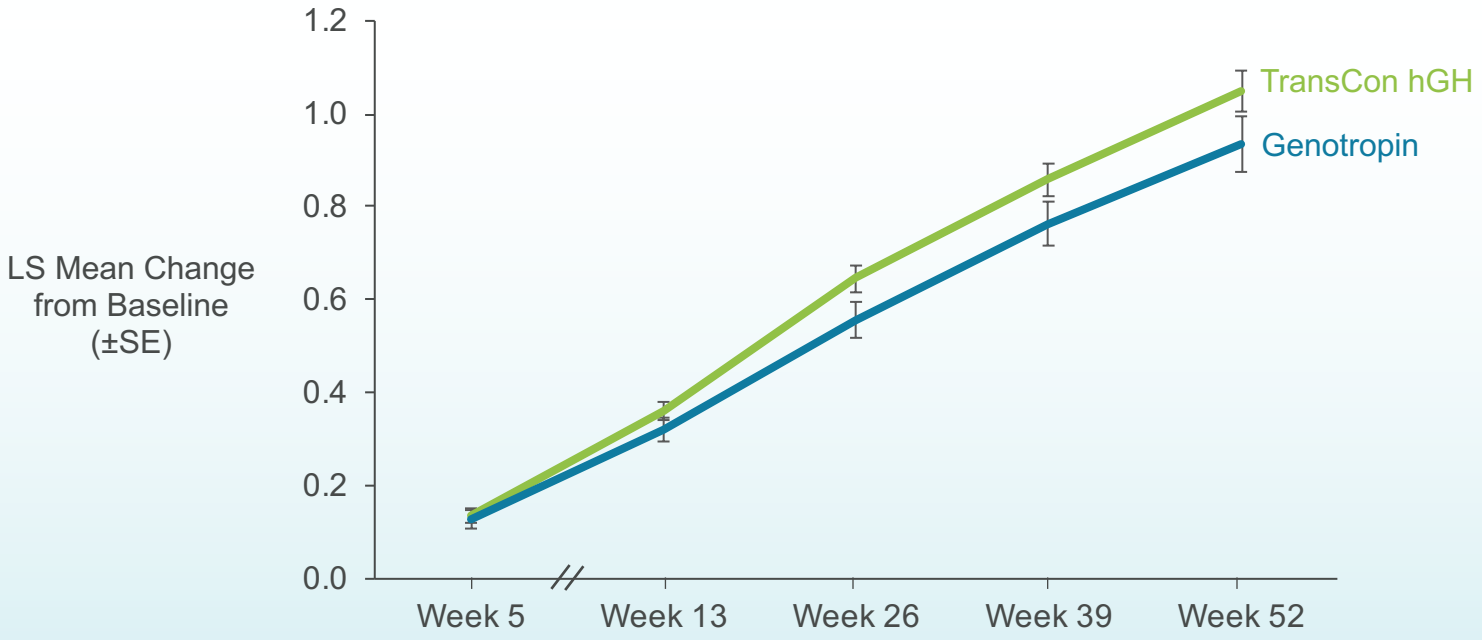
TransCon hGH Met Primary Objective of Non-inferiority and Demonstrated Superiority in AHV at Week 52

	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.

Change in Height SDS Demonstrated an Increasing Difference



MMRM model.

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)

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

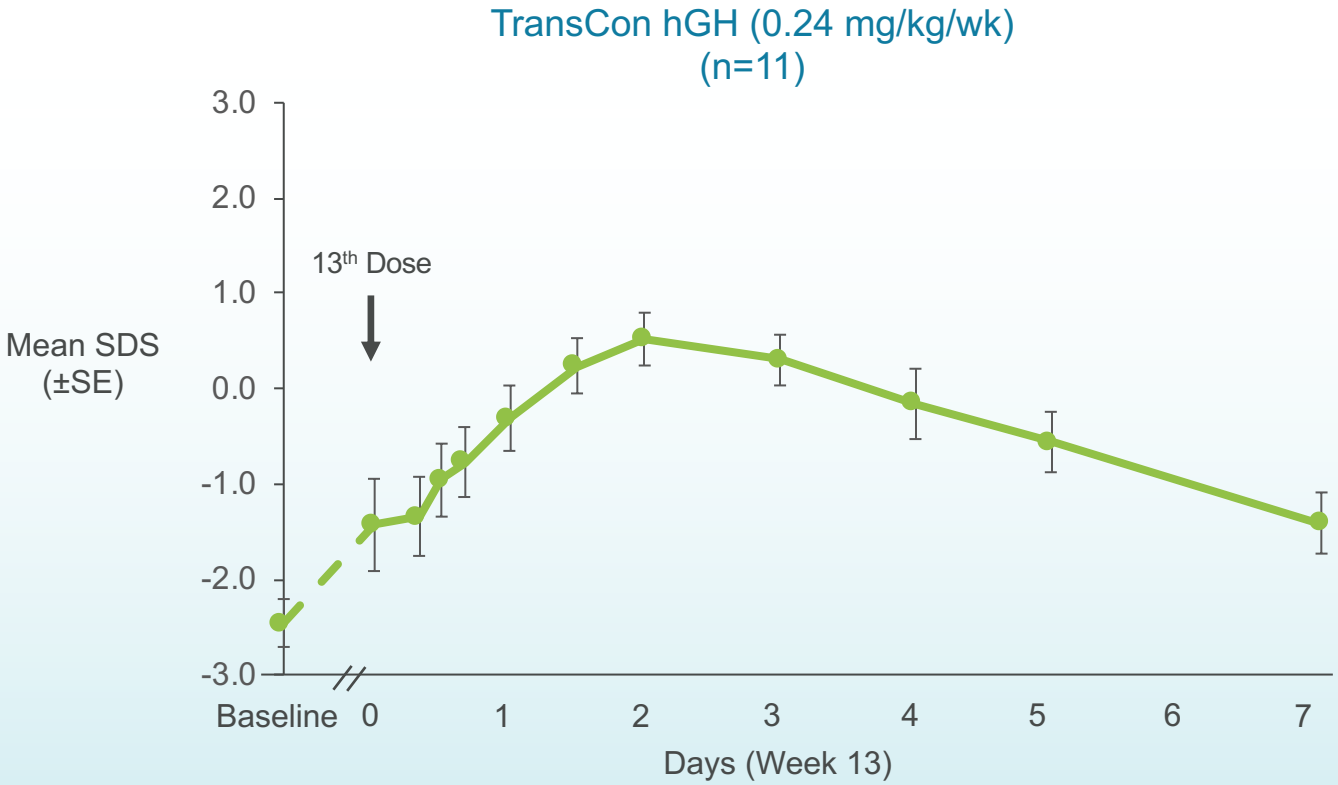
IGF-1 levels increased with TransCon hGH

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.

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

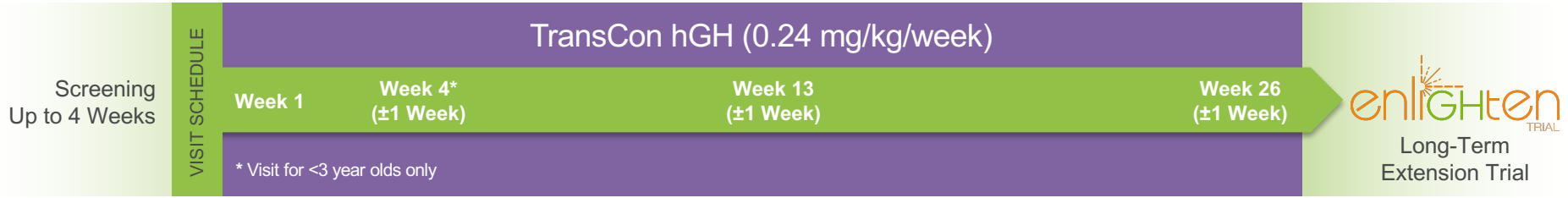
IGF-1 Profile Over 1 Week



Phase 3 fliGHt Trial Design

fliGHt TRIAL

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

Top-line results from phase 3 fliGHt Trial.

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%)

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

Top-line results from phase 3 fliGHt Trial.

Key Learnings from TransCon hGH Clinical Trials

- TransCon hGH demonstrated a safety profile comparable to that of a daily hGH
- TransCon hGH demonstrated superior efficacy[1] to a daily hGH through a PK profile of released hGH that may be more efficiently utilized by target tissues
- TransCon hGH data showed predictable response to dose titrations
- TransCon hGH data suggest the same mode of action as daily hGH and preserved the biological balance between direct hGH and IGF-1 effects in target tissues

[1] Based on results from phase 3 heiGHt Trial

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Safety Profile of TransCon hGH and Daily hGH[1]

	heiGHt Trial		fliGHt Trial	Phase 2 Trial[2]			
	TransCon hGH 0.24 (n=105) n (%)	Genotropin 0.24 (n=56) n (%)	TransCon hGH 0.24 (N=146) n (%)	TransCon hGH 0.14 (n=12) n (%)	TransCon hGH 0.21 (n=14) n (%)	TransCon hGH 0.30 (n=14) n (%)	Genotropin 0.21 (n=13) n (%)
Treatment-emergent Adverse Events (TEAEs)	81 (77)	39 (70)	83 (57)	7 (58)	6 (43)	8 (57)	8 (62)
TEAEs Related to Study Drug	12 (11)	10 (18)	6 (4.1)	1 (8.3)	0	1 (7.1)	0
Serious Adverse Events (AEs)	1 (1.0)	1 (1.8)	1 (0.7)[3]	1 (8.3)	0	0	0
Serious AEs Related to Study Drug	0	0	0	0	0	0	0
TEAEs Leading to Any Action on Study Drug	2 (1.9)	1 (1.8)	2 (1.4)	0	0	0	0
TEAEs Leading to Discontinuation of Study Drug	0	0	0	0	0	0	0

TransCon hGH was well tolerated with a safety profile comparable with daily hGH

[1] All doses expressed in mg/kg/week
[2] Conducted with an earlier bioequivalent version of TransCon hGH
[3] One subject reported two serious AEs; both considered unrelated to study drug

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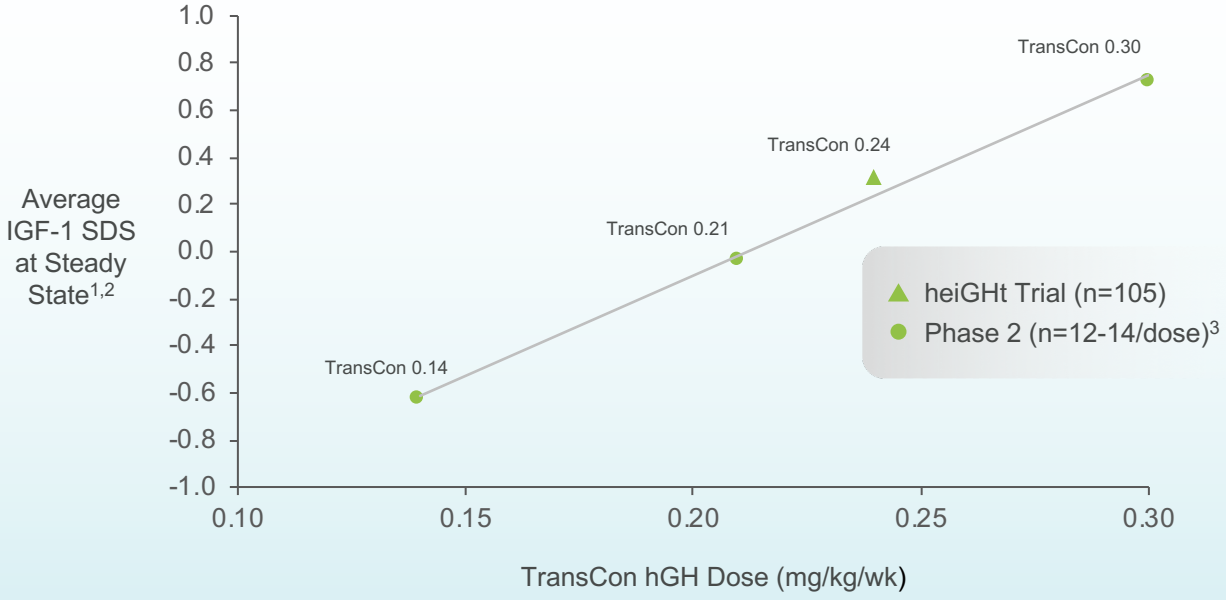
Linear Relationship Between Dose and Average IGF-1 Response Demonstrated in Clinical Program

Average IGF-1 SDS vs TransCon hGH Dose



TransCon hGH data support predictable dose titration

[1] Average IGF-1 at Week 13 was used given availability of measured data over one week for the phase 2 trial
[2] Average IGF-1 during Week 13 for phase 3 heiGHt Trial TransCon hGH subjects is model-derived average
[3] Conducted with an earlier bioequivalent version of TransCon hGH

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TransCon hGH: Data in Previously-Treated Patients Demonstrated Predictable Responses to Titration

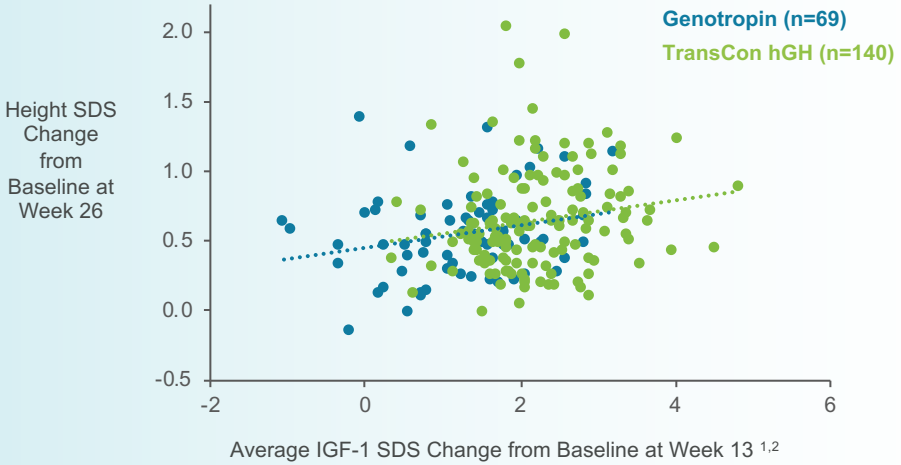
	TransCon hGH
Patients with down-titration(s)	n=29
Average dose reduction	0.045 mg/kg/wk
Daily hGH dose (prior to TransCon hGH)	0.28 mg/kg/wk
Baseline IGF-1 SDS (daily hGH), mean (SD)	2.02 (0.99)
Pre-dose reduction IGF-1 SDS, mean (SD)	2.87 (1.04)
Post-dose reduction IGF-1 SDS, mean (SD)	2.46 (1.09)
Post-dose reduction change in average IGF-1 SDS[1]	0.41
Model-predicted[2] change in average IGF-1 SDS	0.38

Predictable linear dose-dependent IGF-1 response observed across clinical trials

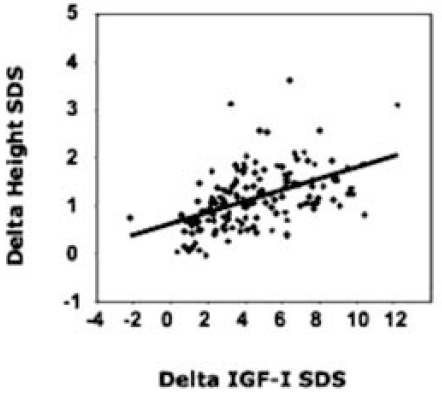
[1] Measured at day 5 ± 1 after dosing
[2] Model based on phase 2 and phase 3 regression data

Relationship Between Average IGF-1 SDS and Height SDS from Phase 2 and Phase 3 Trials

TransCon hGH subjects from phase 2 and phase 3 trials combined



Published two-year data from controlled trial with daily hGH in the U.S. (N=172)[3]



Similar slopes for Genotropin and TransCon hGH suggest:

- Similar relationship of height SDS and average IGF-1 SDS
- Preservation of the biological balance between direct hGH and IGF-1 effects

[1] Average IGF-1 at week 13 was used given availability of measured data over one week for the phase 2 trial
[2] Average IGF-1 during week 13 for phase 3 heiGHt Trial TransCon hGH subjects is model-derived average
[3] Cohen et al. J Clin Endocrinol Metab 2007, 92(7): 2480-2486

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Auto-Injector Designed to Improve Adherence

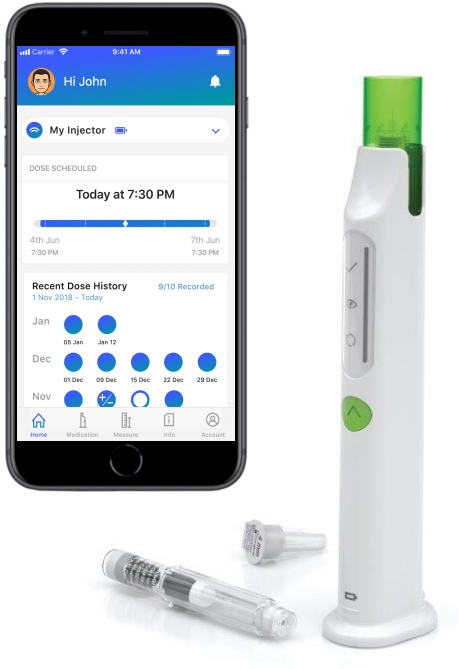
Key Features

- 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

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



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

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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

TransCon PTH:
PTH Replacement Therapy for Hypoparathyroidism

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

Short-term Complications

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

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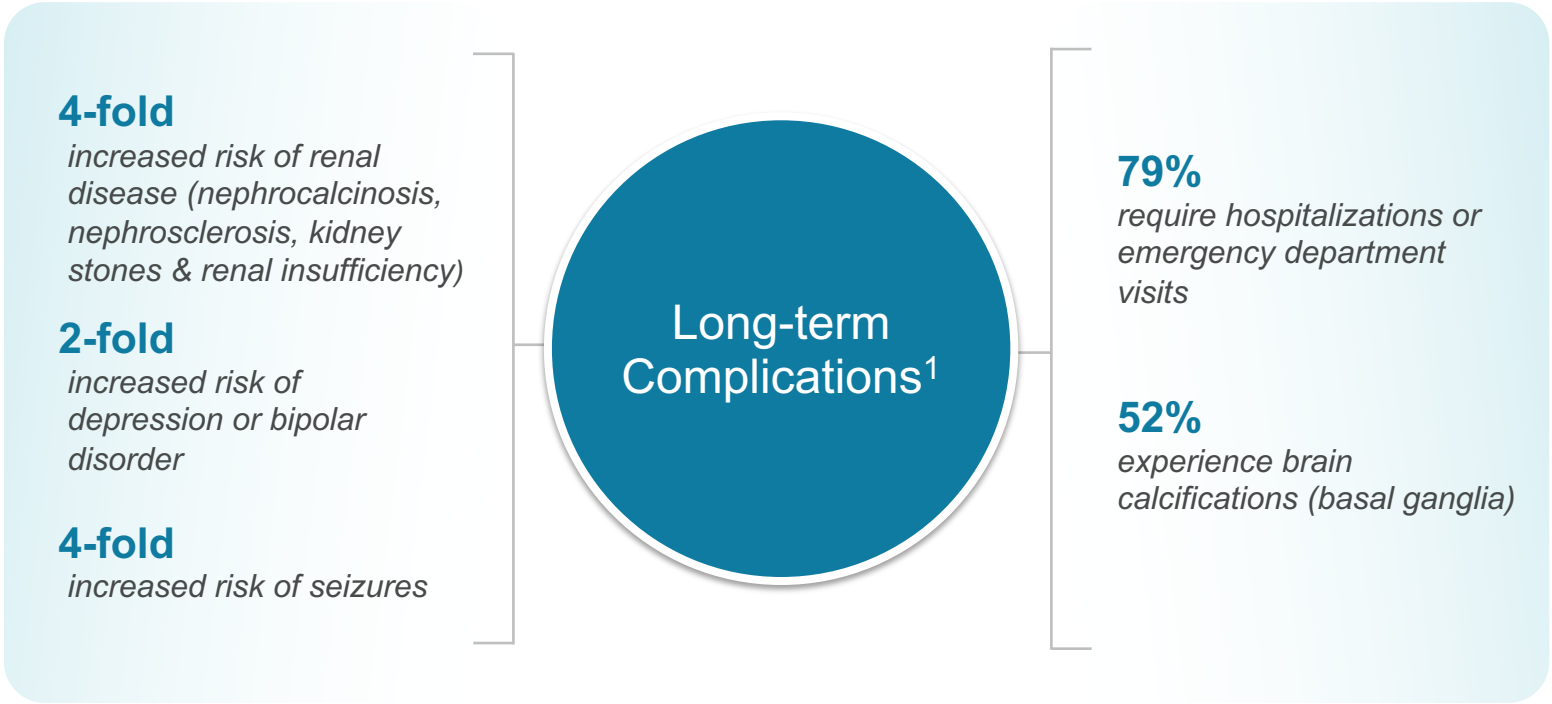
Hypoparathyroidism: Severe Long-term Complications



[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

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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

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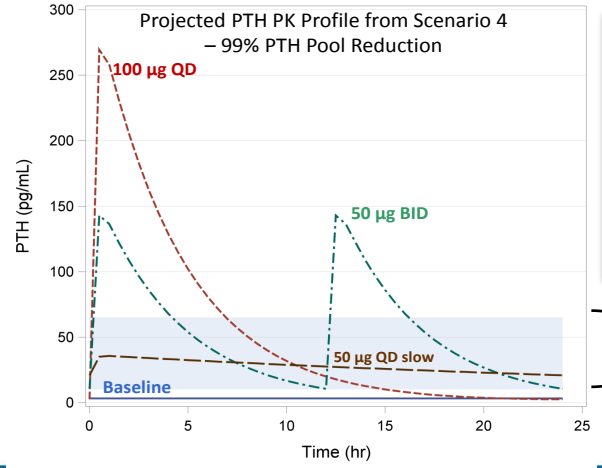
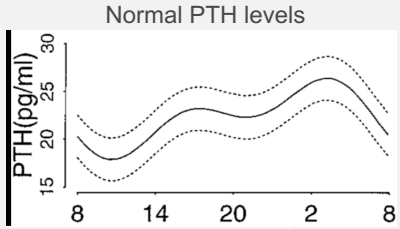
Constant Normal Level of PTH is Optimal - FDA Perspective[1,2]

U.S. Food and Drug Administration
Protecting and Promoting Public Health
www.fda.gov

Altering Regimen (QD to BID) or Release Profile Bring PTH Levels Close to the Physiological Levels





Normal Physiological range (10 -65 pg/mL)*

20

- 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

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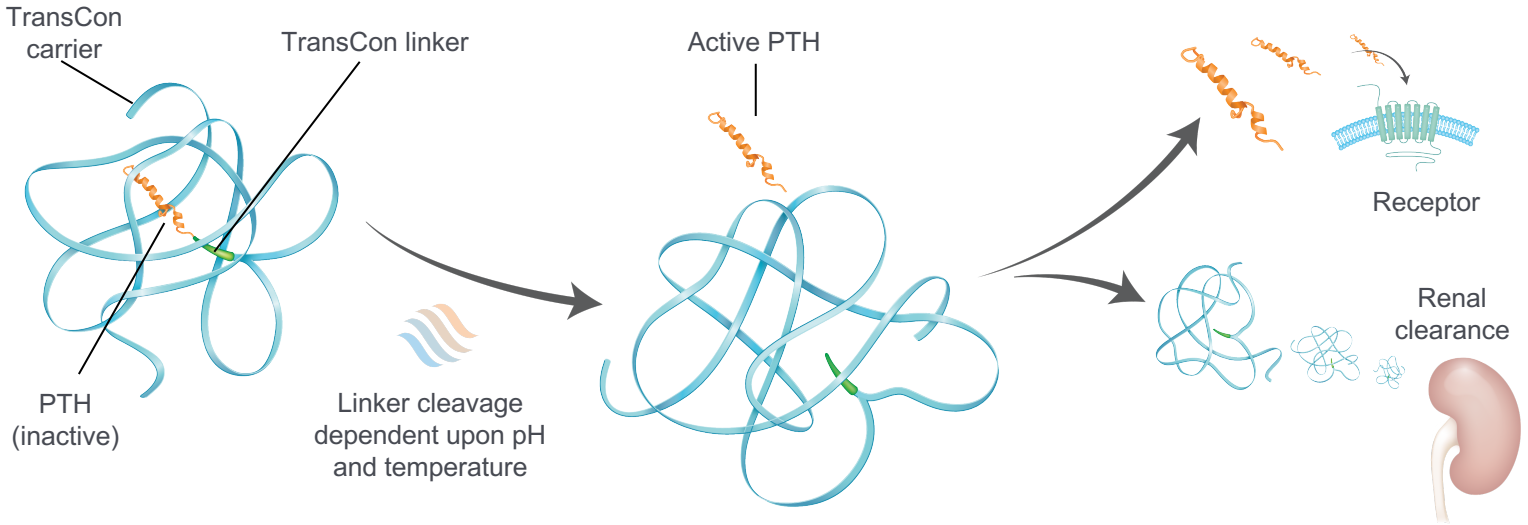
TransCon PTH: Target Profile

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 Design

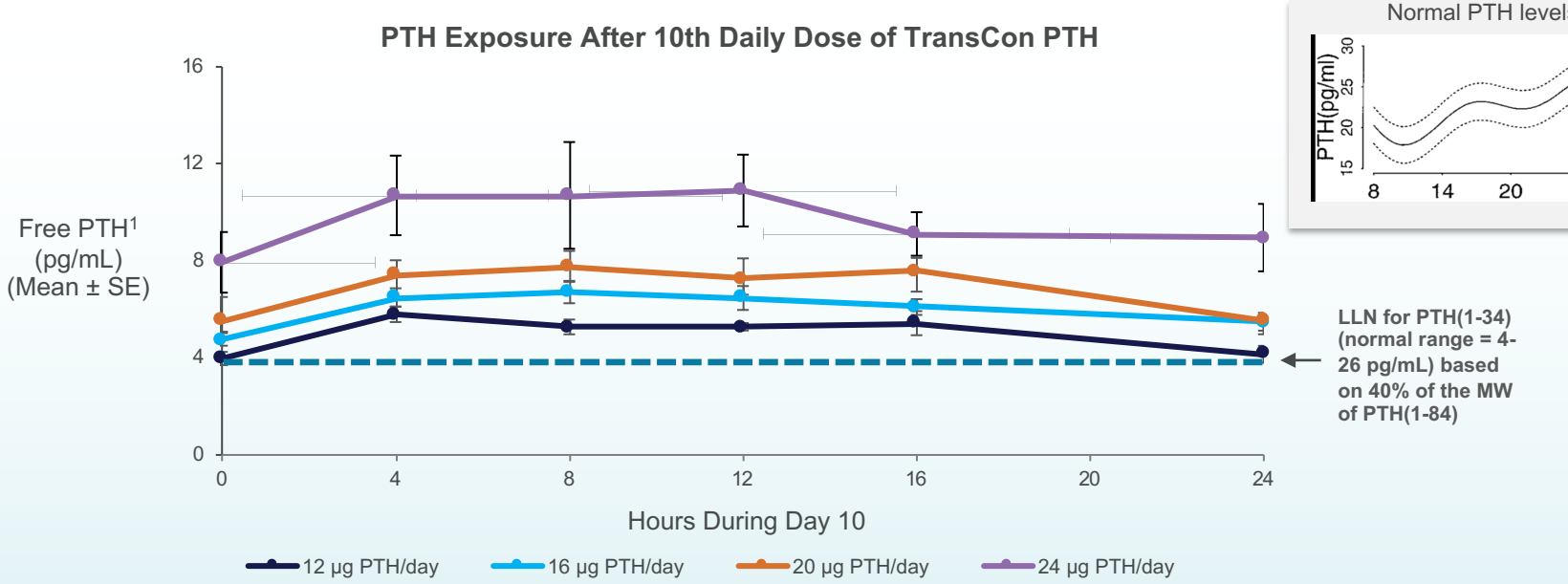


- TransCon PTH is a sustained-release prodrug designed to provide stable PTH levels in the physiological range for 24 hours/day
- TransCon PTH designed to normalize blood and urinary calcium levels, serum phosphate and bone turnover

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

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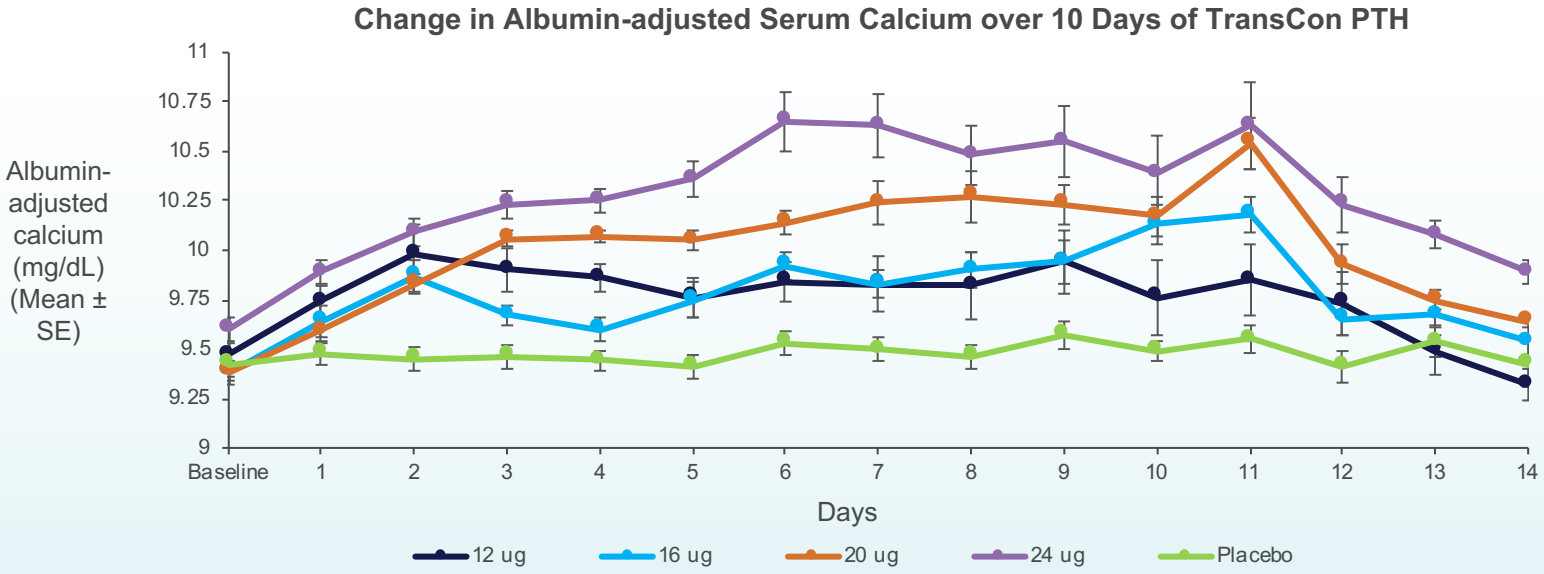
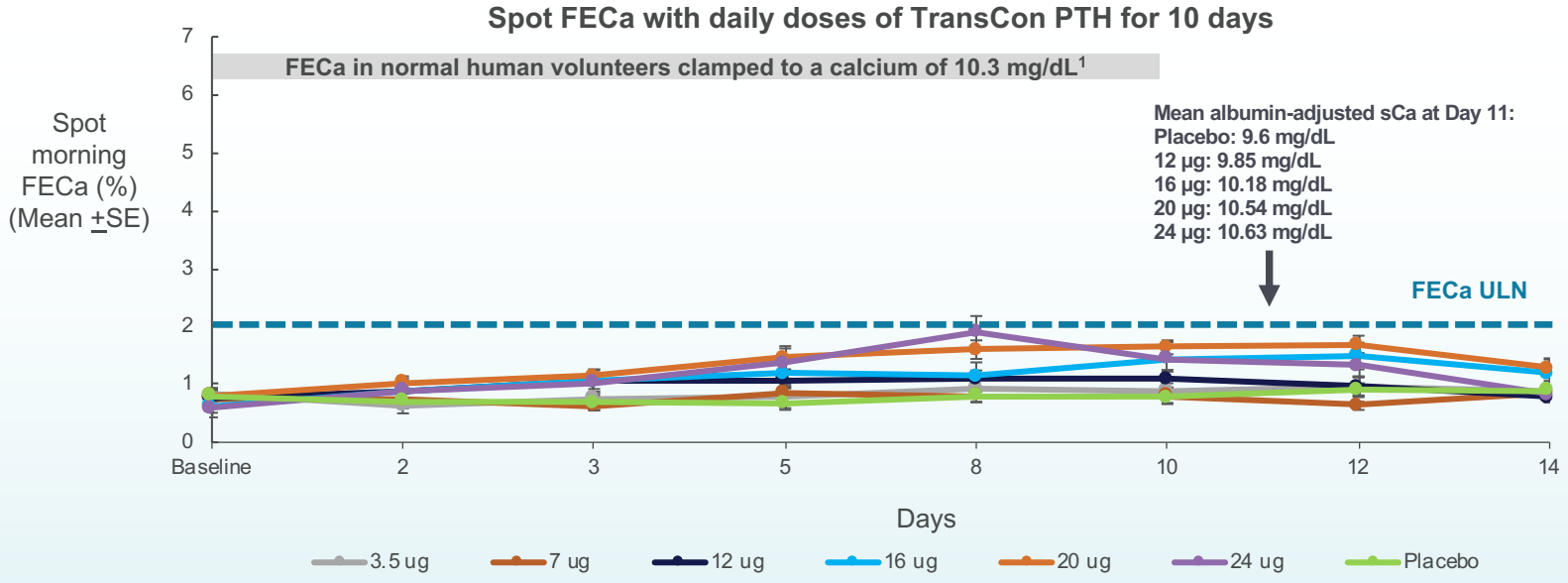
Dose-Dependent Increase of Serum Calcium



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

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

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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)

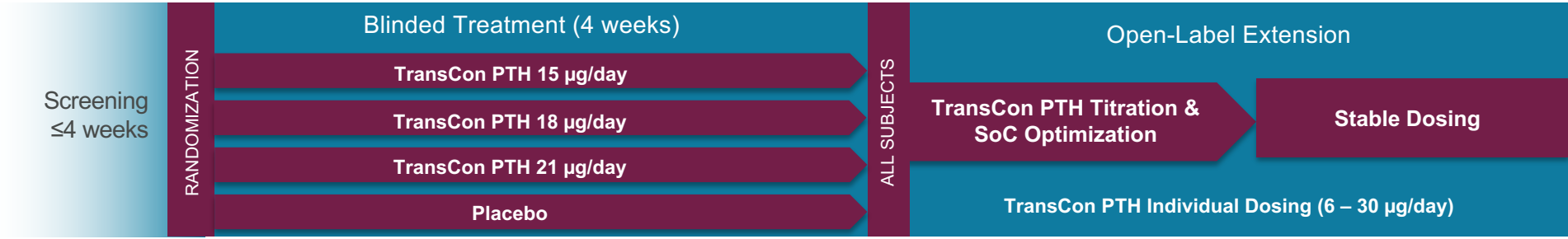
    1 active (12 µg) subject (“catheter site phlebitis”)
  - MAD: 1 placebo subject (“catheter site phlebitis”) (withdrew)

    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 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

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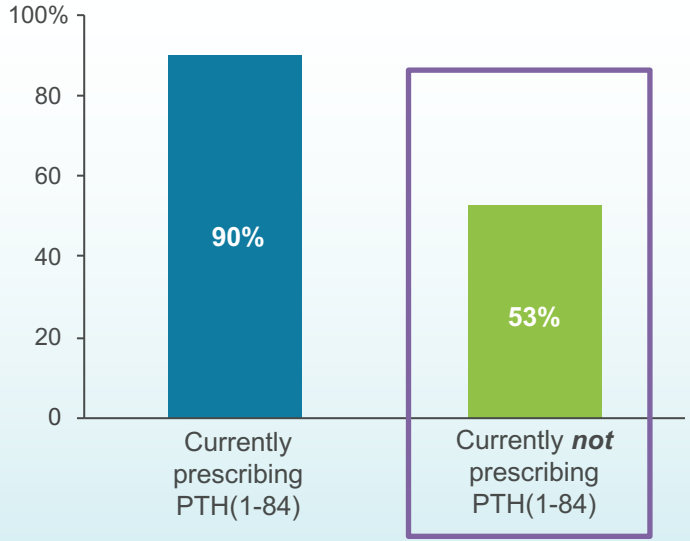
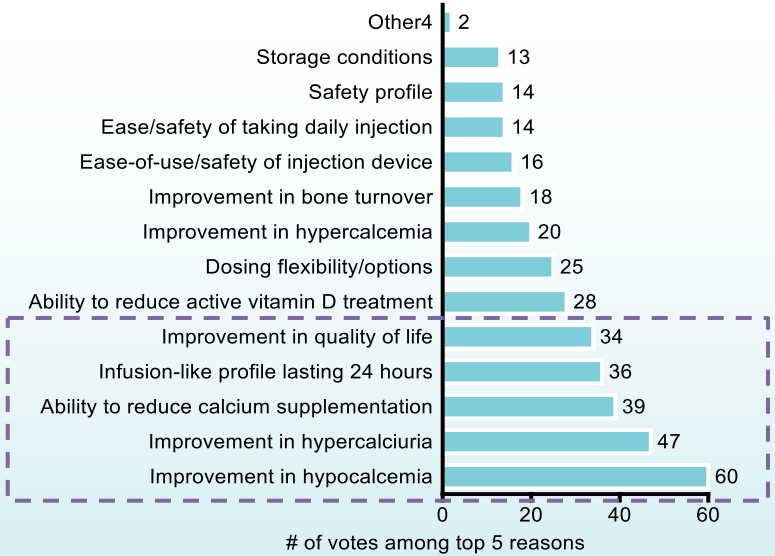
>70% of Physicians Indicate Likelihood to Prescribe TransCon™ PTH[1]

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



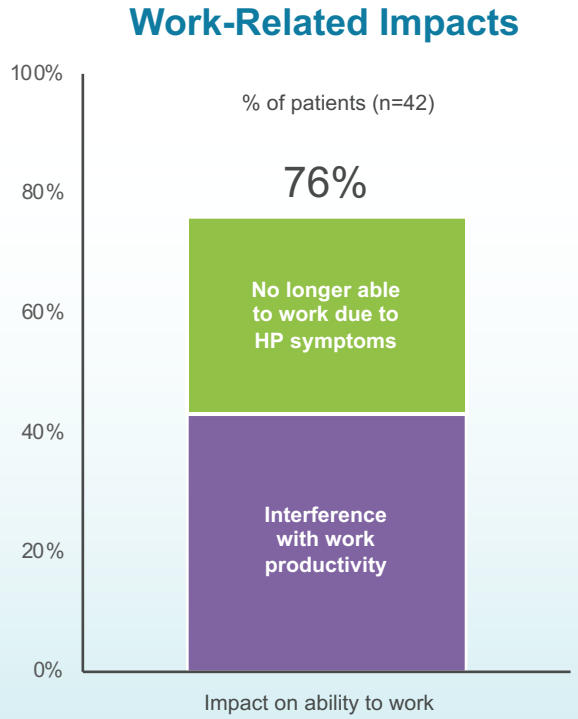
Reasons to Prescribe TransCon PTH[3,4] (n=76)



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.

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

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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: The New Frontier of Growth Biology

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

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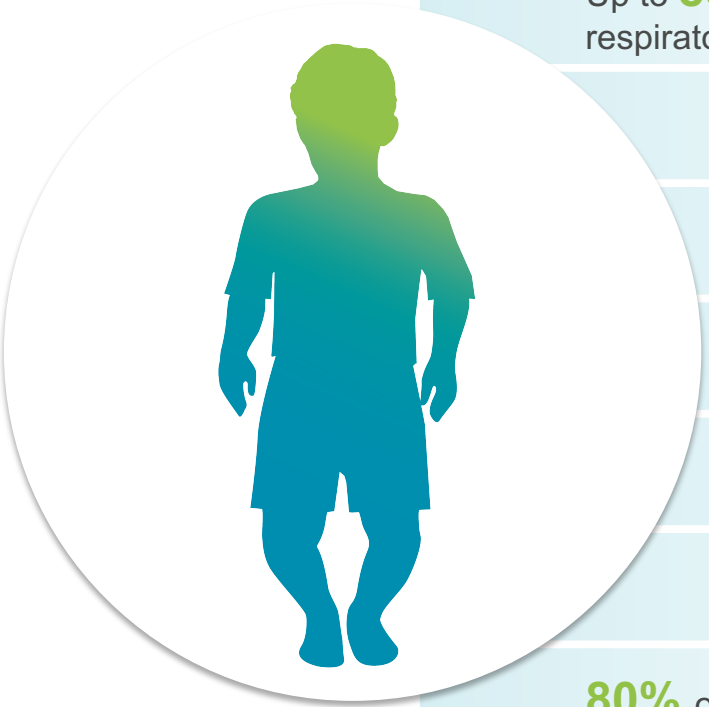
Achondroplasia: High Morbidity



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

The Application of Clinical Genetics, 2014:7117-125

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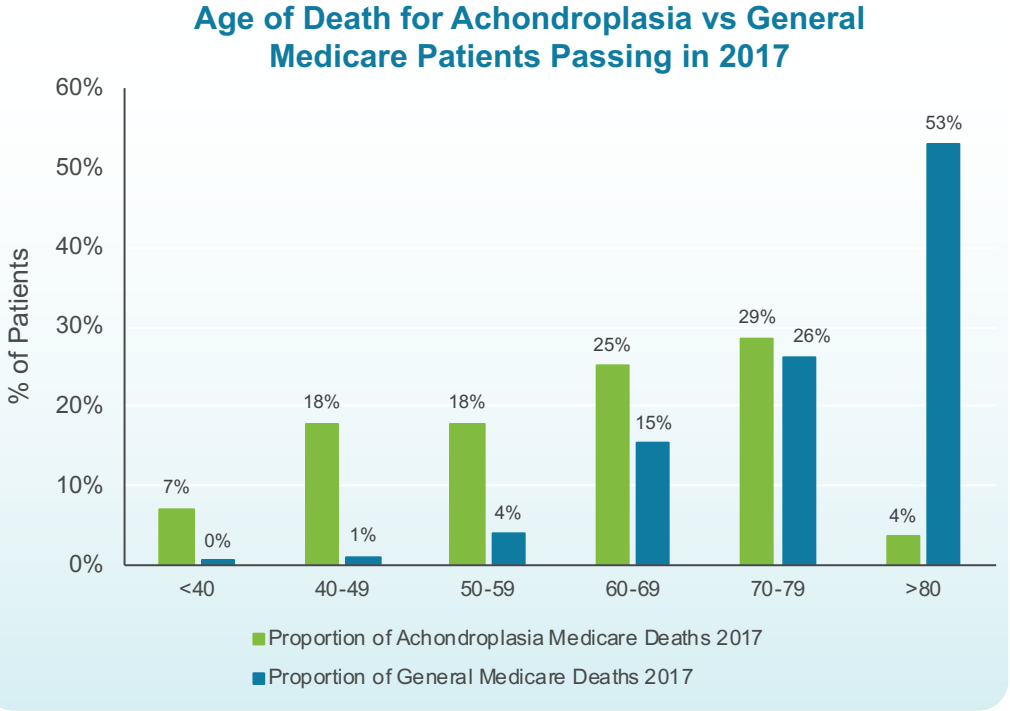
Achondroplasia: Higher Mortality

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.

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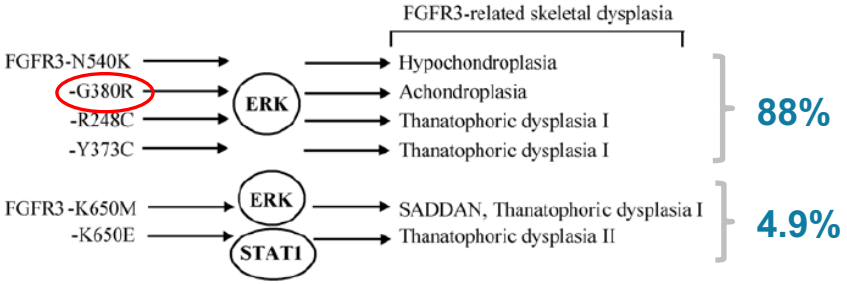
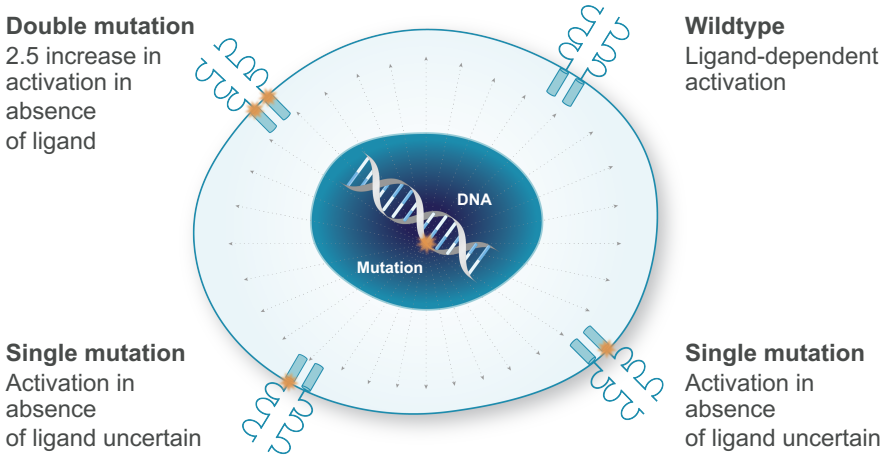
Achondroplasia: Autosomal Dominant Mutation in *FGFR3*

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

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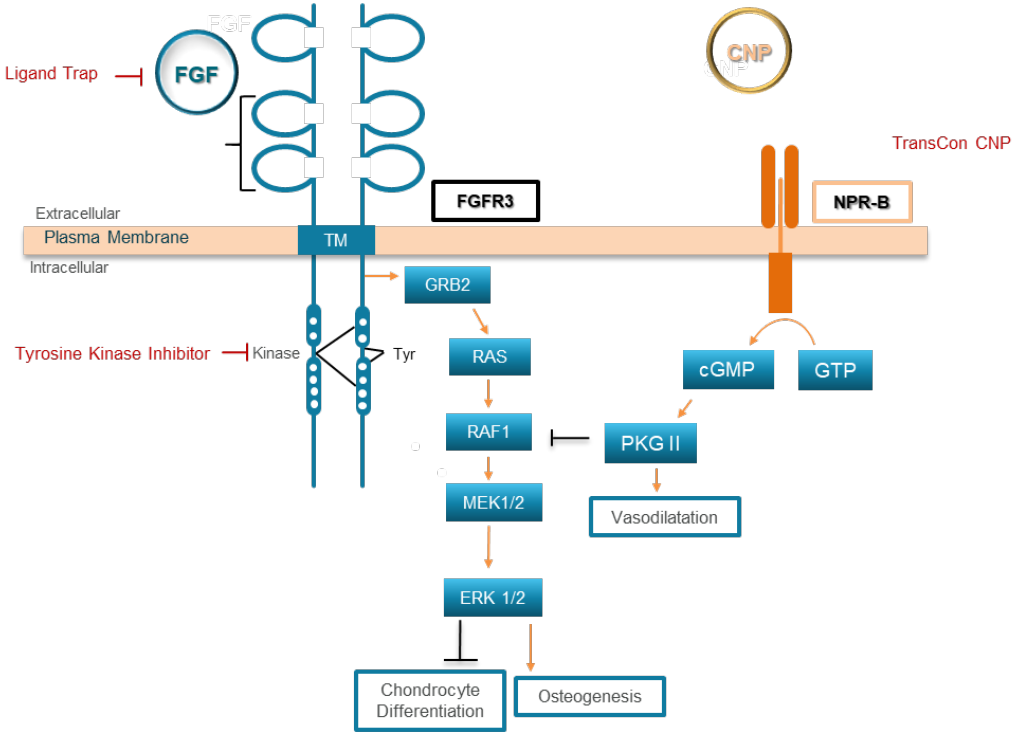
Achondroplasia Signaling Defect is Well Understood[1]

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

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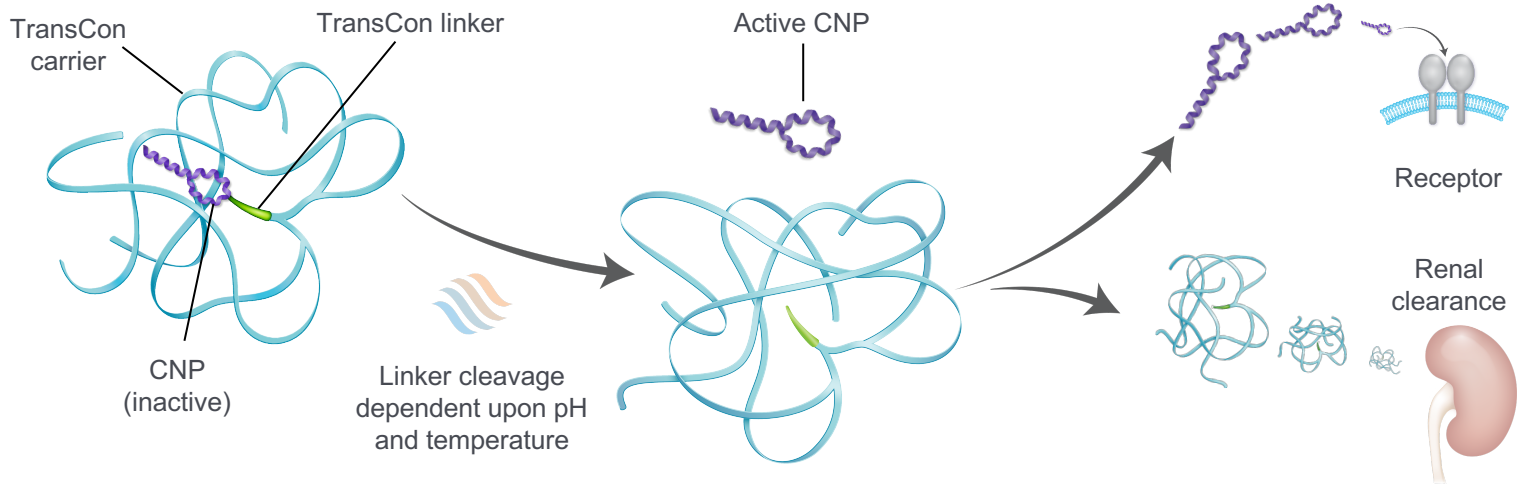
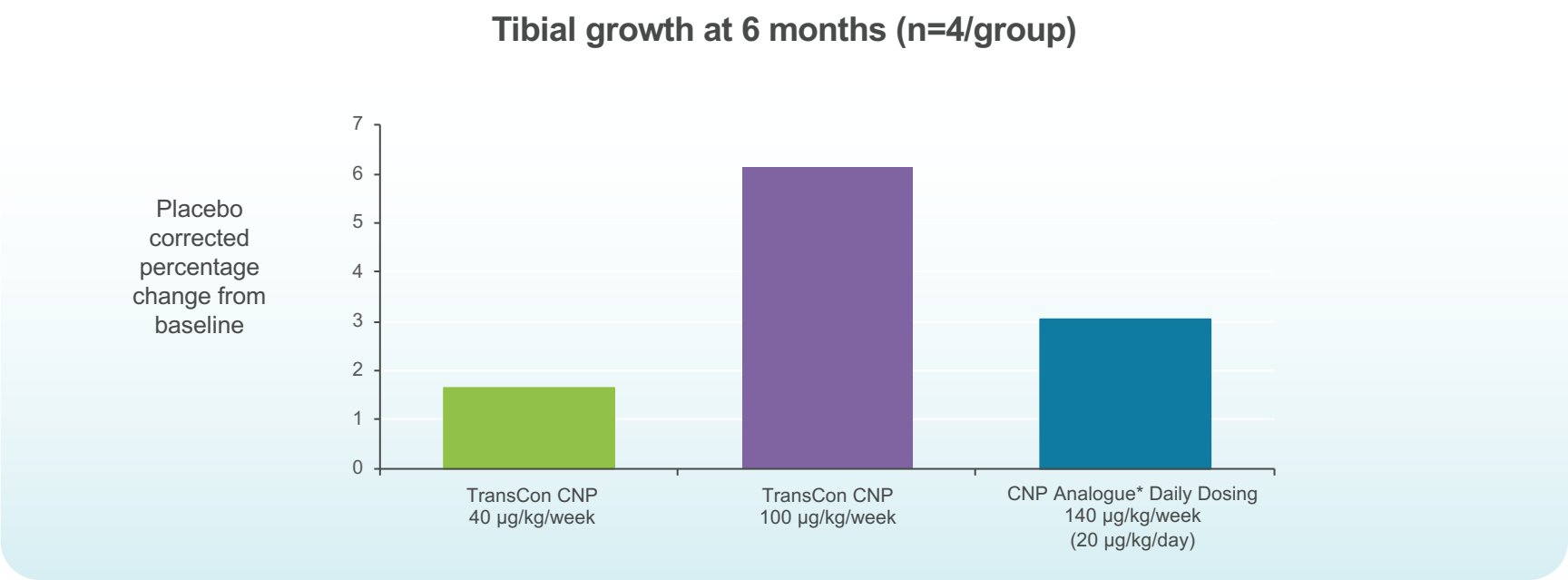
TransCon CNP Design



- 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



- 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)

Each dose tested sequentially starting at lowest dose[1]

Up to 10 subjects randomized in each dose cohort in a blinded manner

3 µg/kg → **10** µg/kg → **25** µg/kg → **75** µg/kg → **150** µg/kg

Data Safety Monitoring Board (DSMB) reviews blinded data after each dose cohort and approves escalation to next dose

Dosing assignments unblinded after DSMB review

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.

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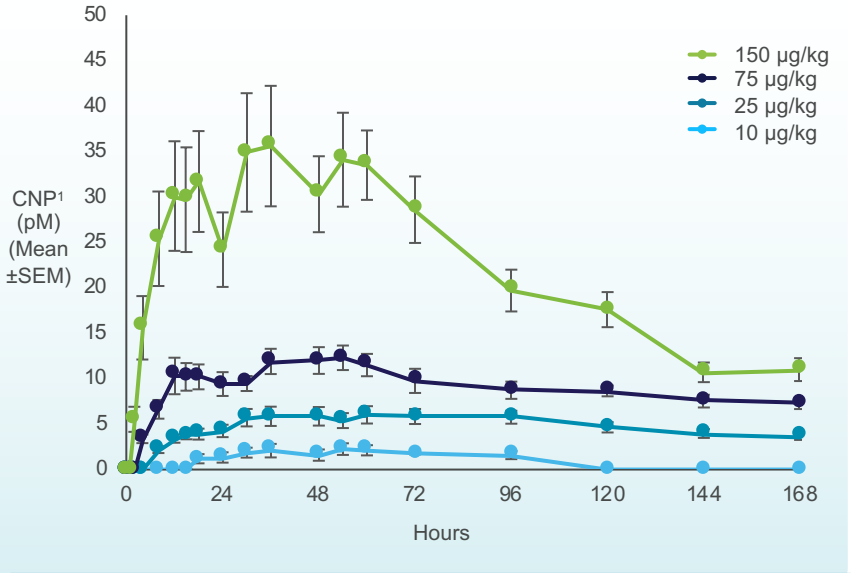
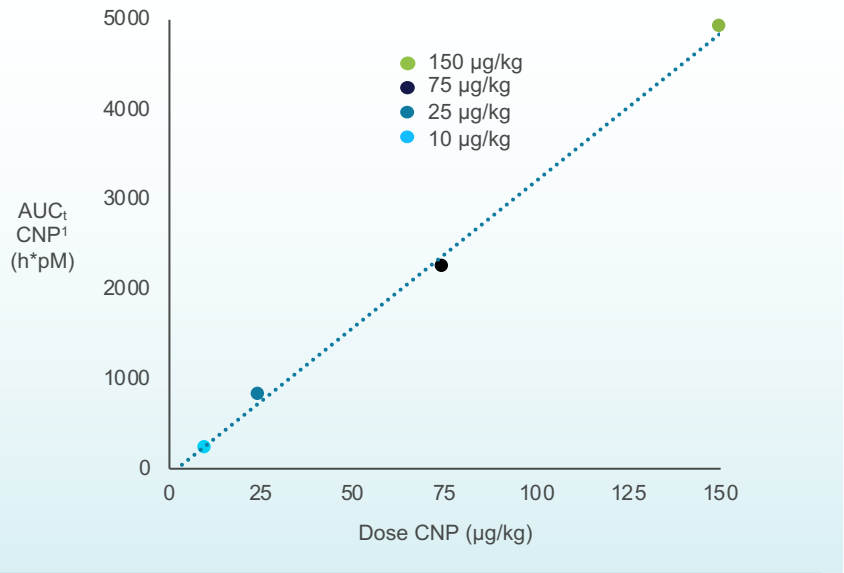
Dose Proportional CNP Exposure For 1 Week

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



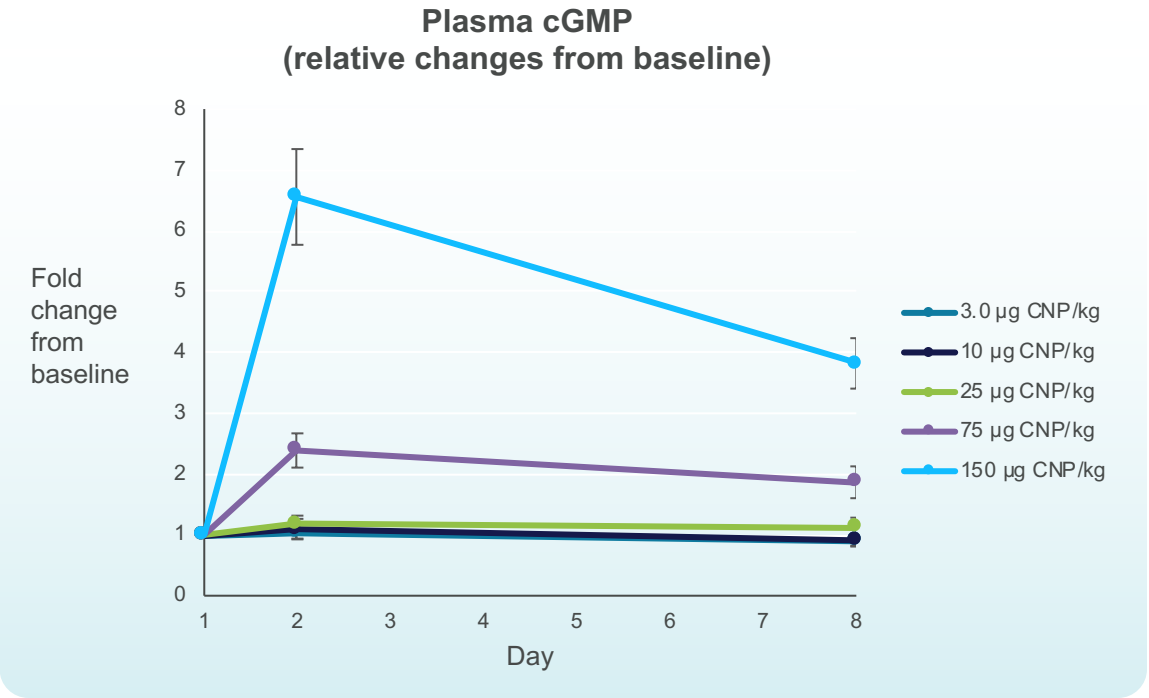


- Dose proportional increase in CNP exposure suggests ability to titrate dosing
- Phase 1 showed effective CNP $t_{1/2}$ of approximately 120 hours (native CNP $t_{1/2}$ of 2-3 minutes)

[1] CNP measured as CNP-38

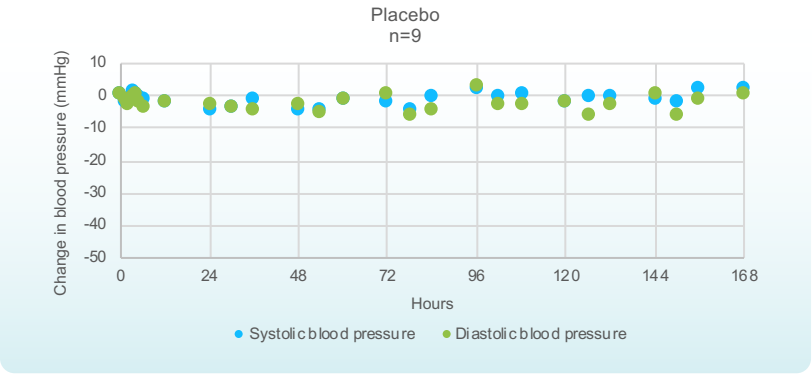
Dose Dependent cGMP[1] Response Demonstrated Receptor Engagement For 7 Days

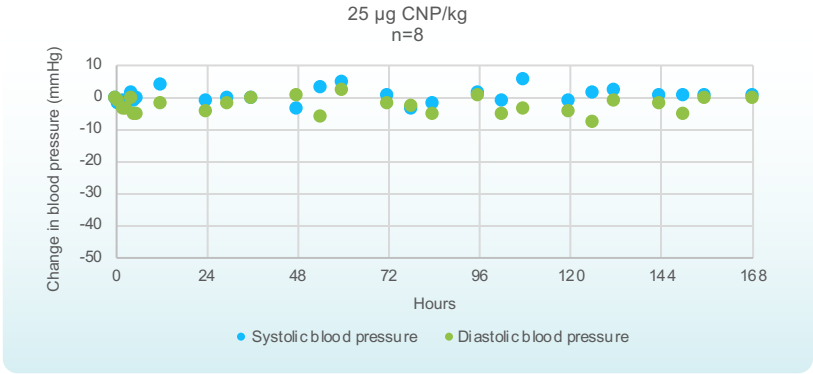
- cGMP is a secondary messenger of NPR-B activation by CNP
- cGMP levels correlate with TransCon CNP PK profile

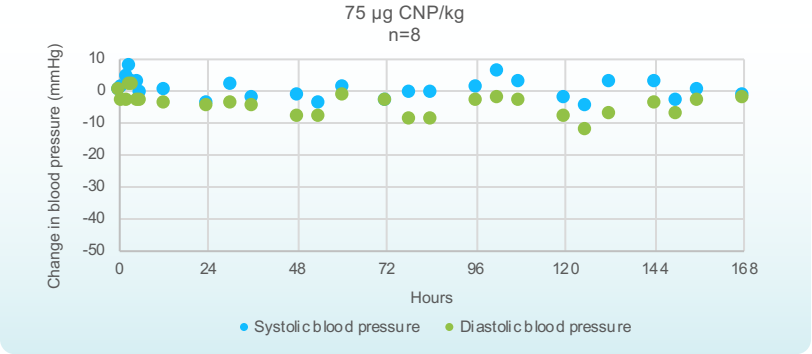


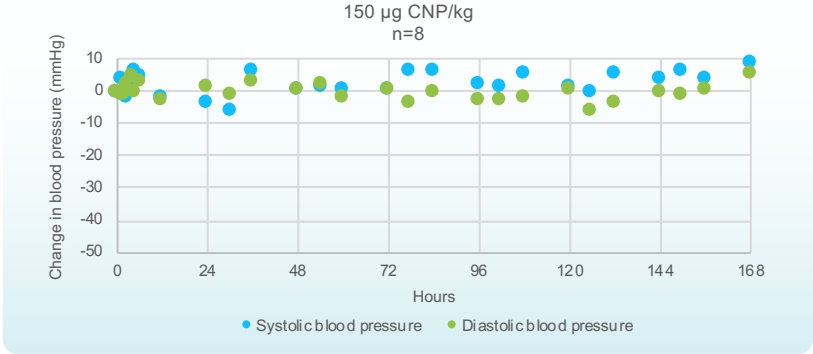
[1] cGMP=cyclic guanosine monophosphate.

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

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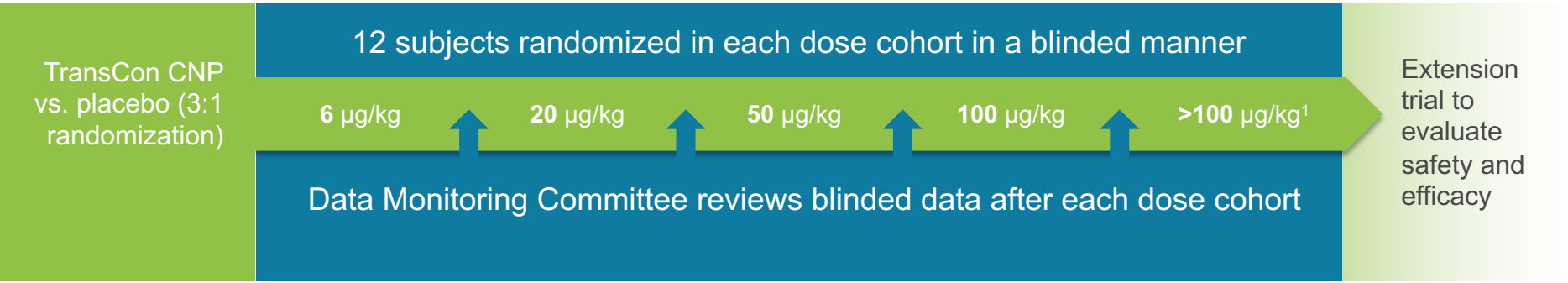
TransCon CNP: Preliminary Phase 2 Trial Design

ACcomplisH TRIAL

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



Primary Endpoint

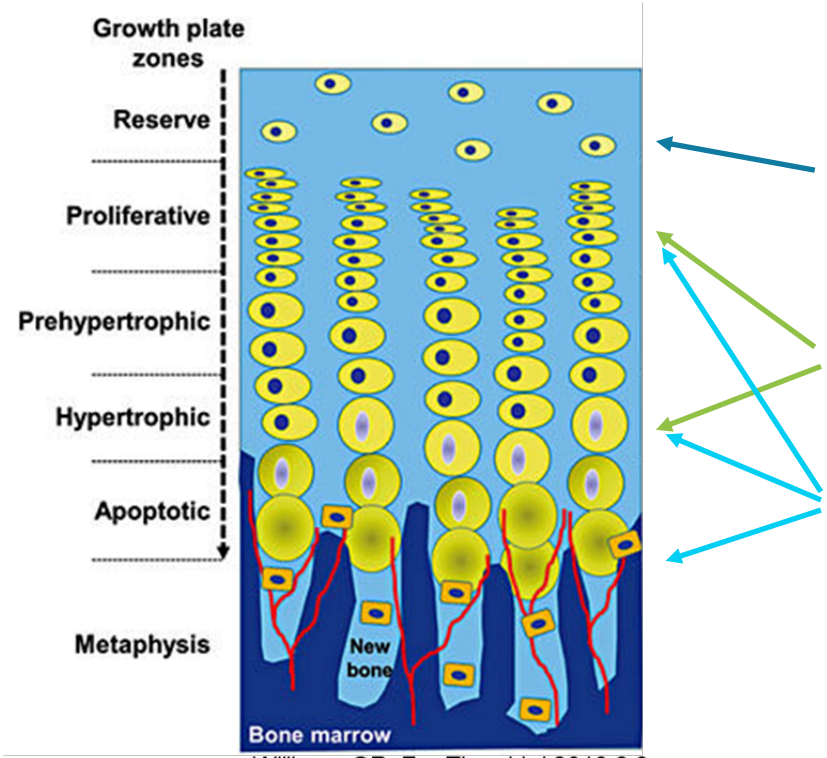
- Annualized height velocity, as measured after 12 months of weekly TransCon CNP treatment

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.

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.

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; ACcomplisH phase 2 trial initiated
- Potential to pursue other growth disorders as monotherapy and in combination with TransCon hGH

Oncology

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

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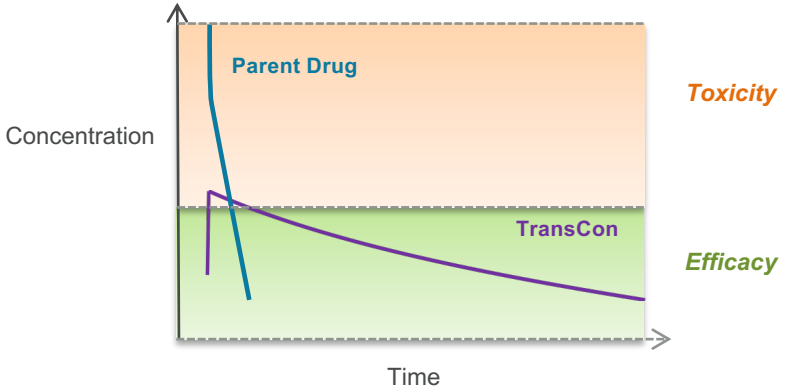
Positioned to Make a Dramatic Impact in Oncology

- 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

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***

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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

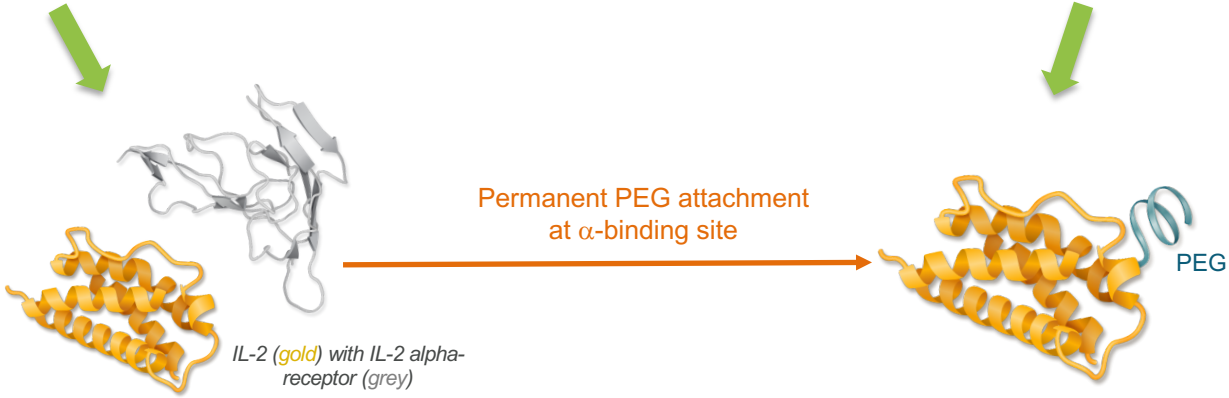
Design of IL-2 β/γ: Site-selective PEGylation for Permanent Receptor Selectivity and Optimized Potency

Generation of IL-2 Variant

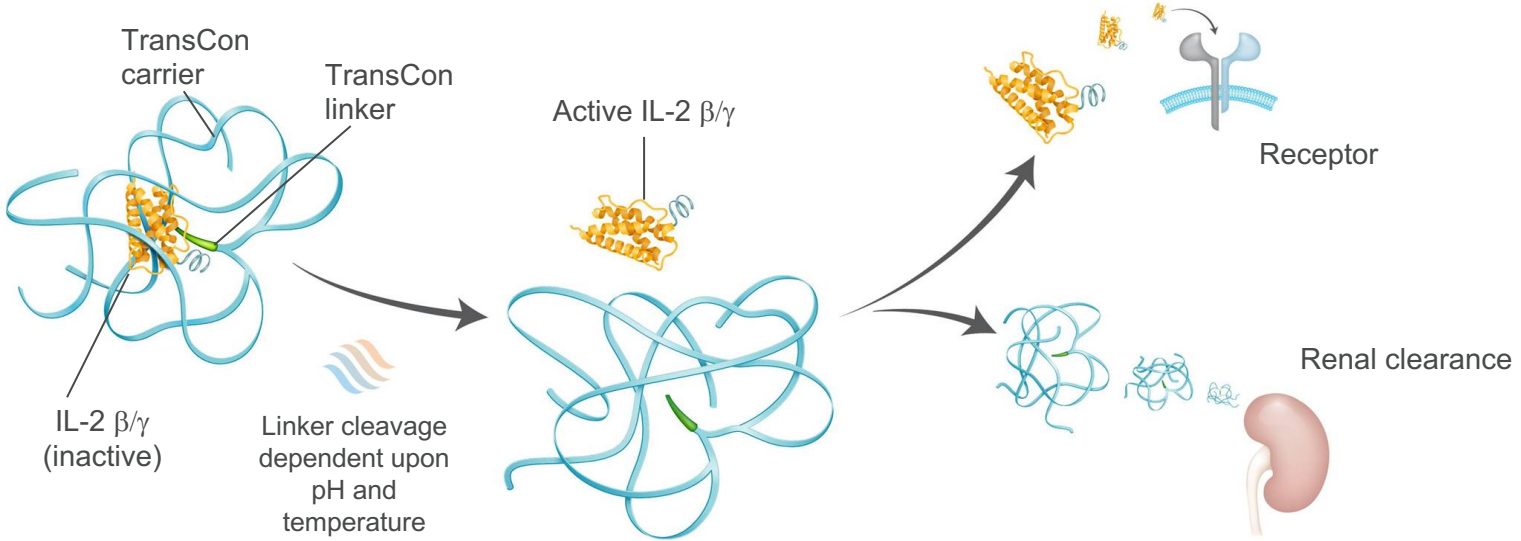
Introduction of cysteine at α–binding site of IL-2

Blocking α–binding

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



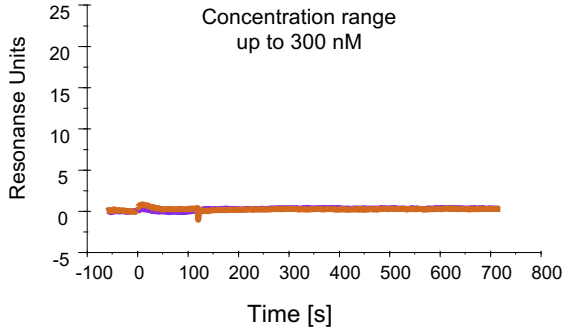
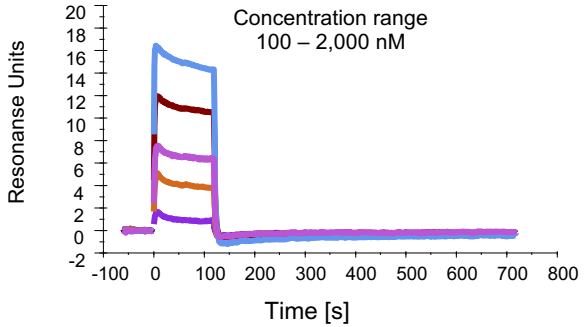
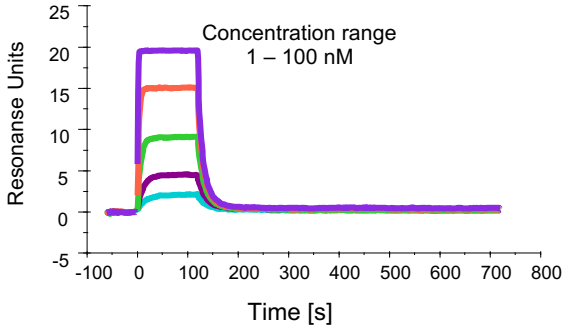
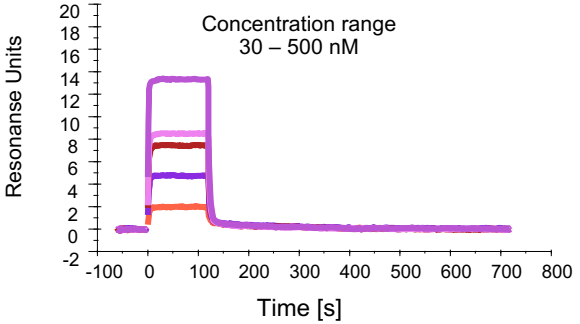
Design of TransCon IL-2 β/γ



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

	Binding to IL-2R α-chain	Binding to IL-2R β-chain
IL-2 β/γ		
Wild-type IL-2 (aldesleukin seq)		

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

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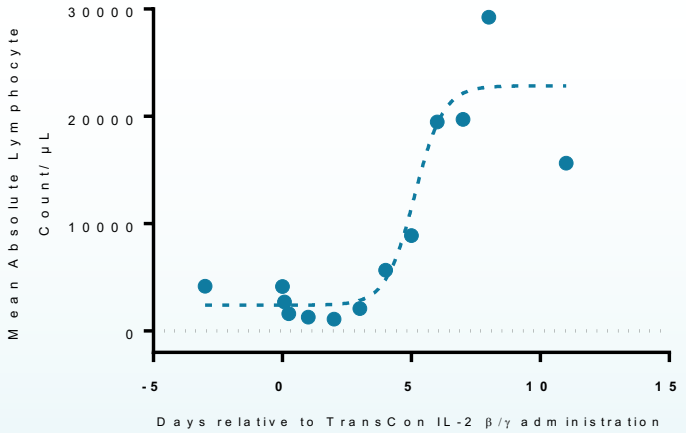
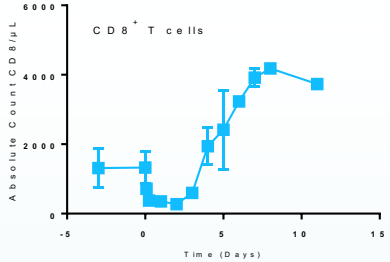
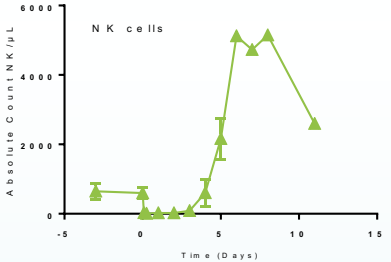
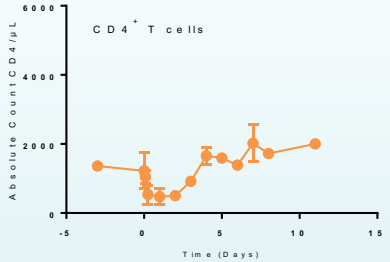
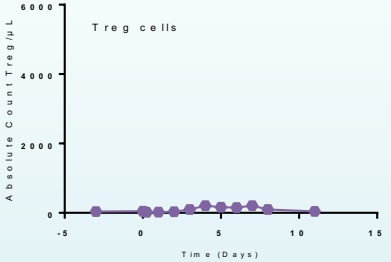
Single Dose of TransCon IL-2 β/γ Increased Levels of Circulating CD8+ T cells and NK cells in Cynomolgus Monkeys









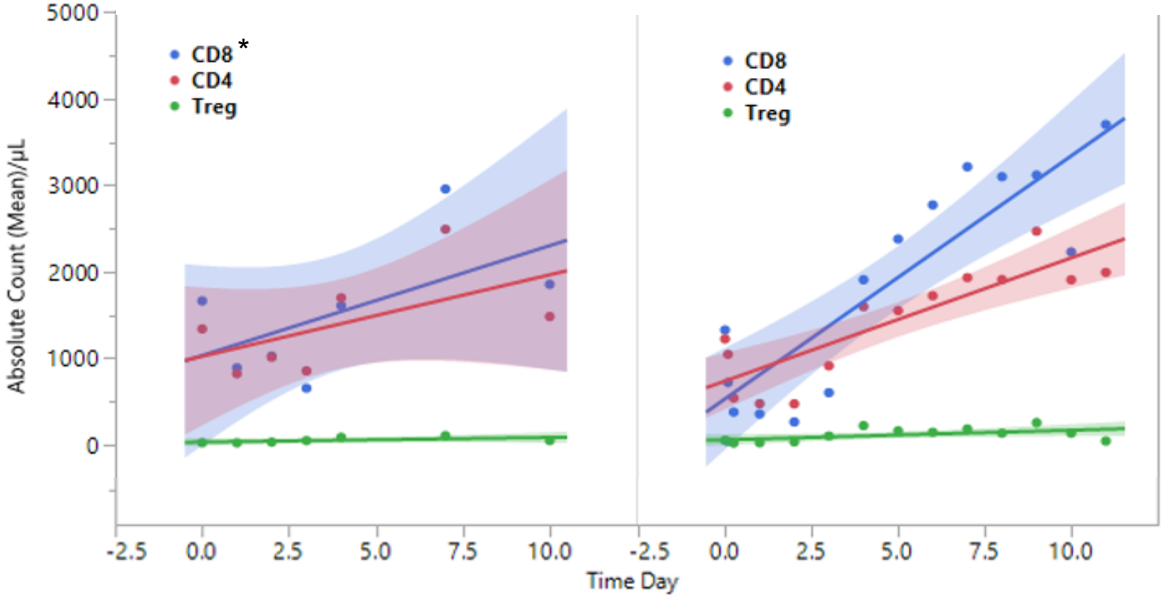


Compound Name	Sex/Weight	Dose (*mg/animal*)	Dosing frequency
TransCon IL-2 β/γ	M/9.2 kg M/8.9 kg M/9.0 kg	0.5 1.0 1.5	Once on Day 0

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)



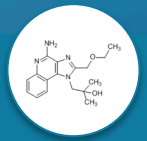
TransCon IL-2 β/γ well tolerated:

- 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.

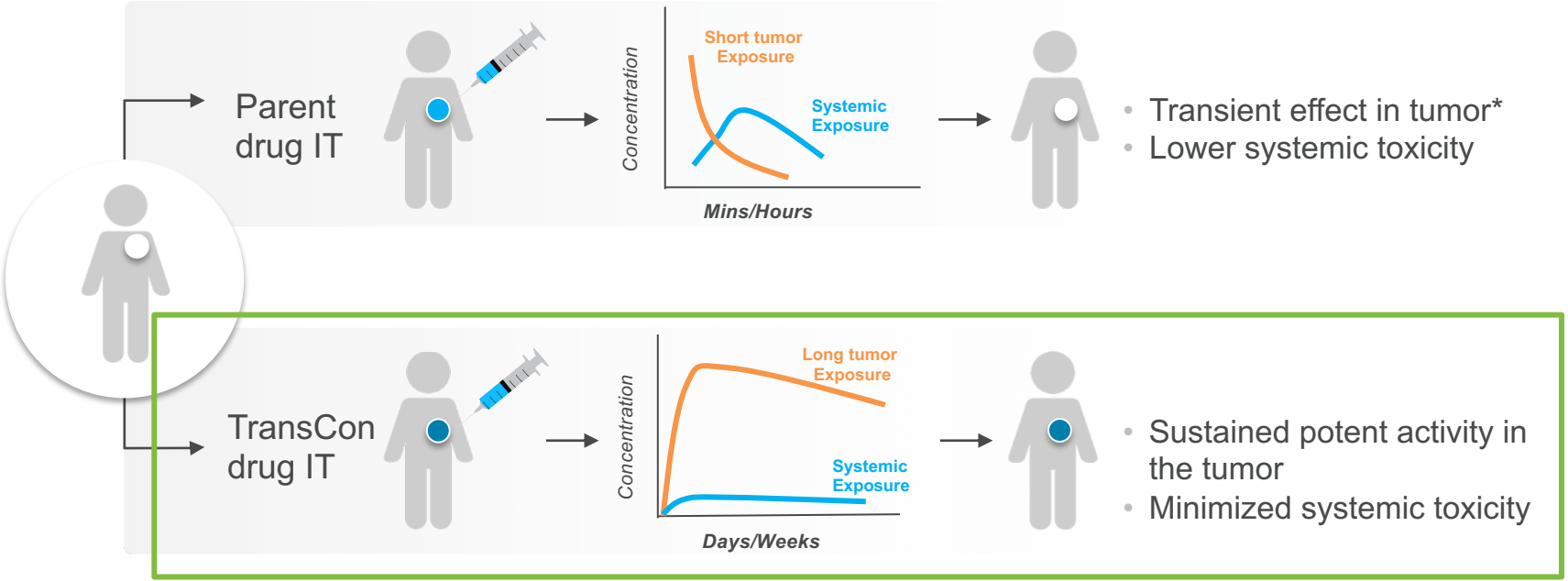
Product Candidates in Oncology



TransCon TLR 7/8 Agonist

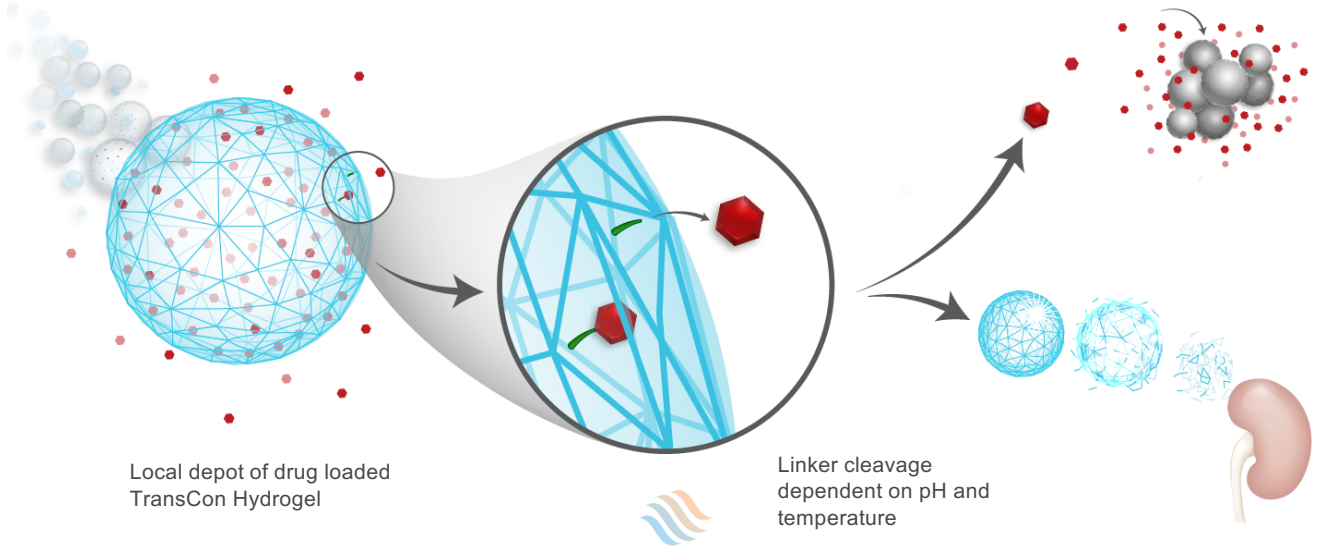
Potential to Transform Efficacy, Safety and Practicality of Intratumoral Treatments

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



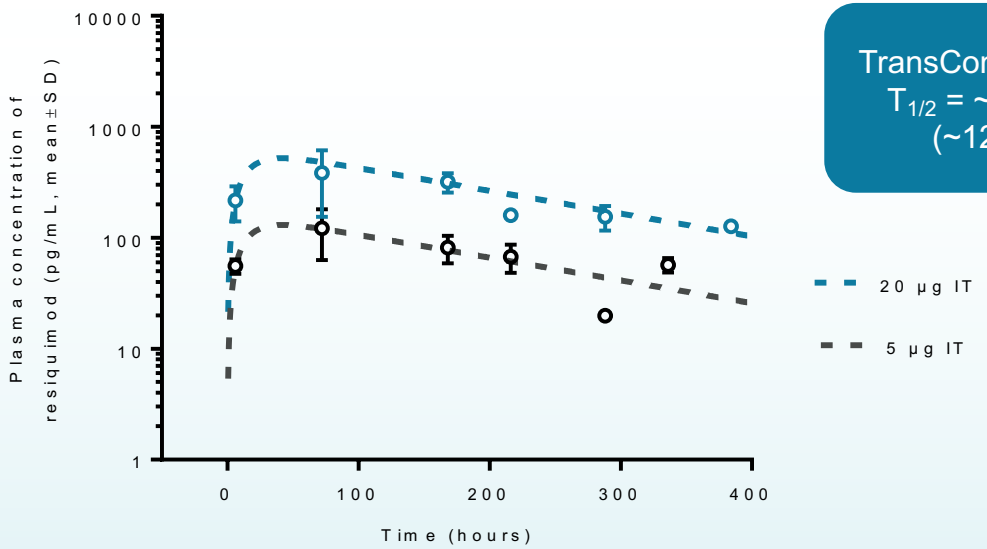
* Example: STING agonist “plasma half-life ranging from 8 to 28 min” (Meric-Bernstam, ASCO, 2019)

Resiquimod Loaded onto TransCon Hydrogel for Intratumoral Sustained Delivery



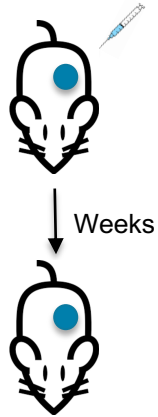
- Resiquimod transiently conjugated to TransCon Hydrogel carrier, designed to provide sustained local release of unmodified parent drug
- Designed to provide sustained activation of tumoral myeloid lineages driving tumor antigen release/presentation and induction of immune stimulatory cytokines

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



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

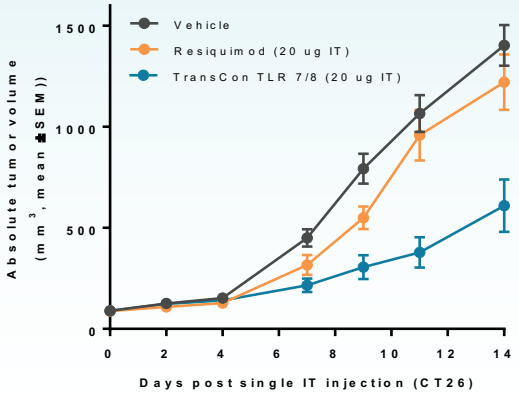
IT injection of TransCon TLR 7/8 Agonist



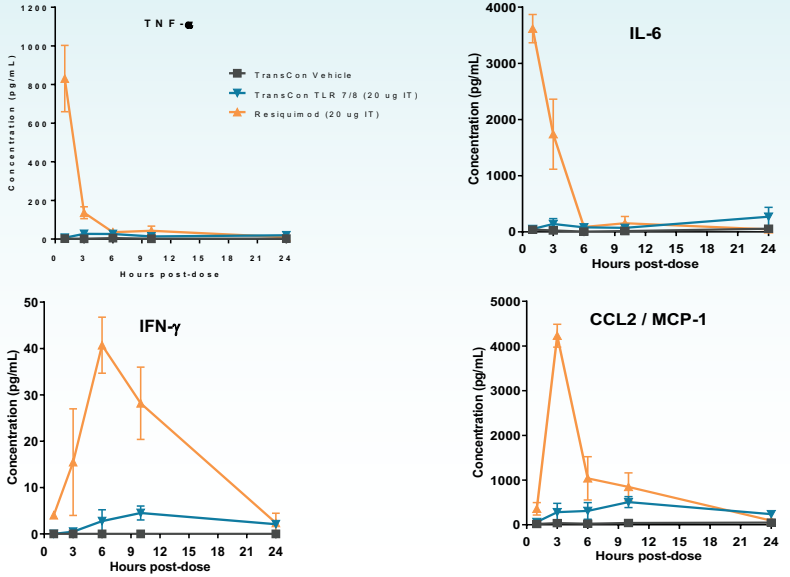
- A single 5 or 20 ug IT dose into CT26 tumors (~0.25 mg/kg or 1 mg/kg)
- The plasma concentration-time profiles were modeled simultaneously with a unified set of parameters

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

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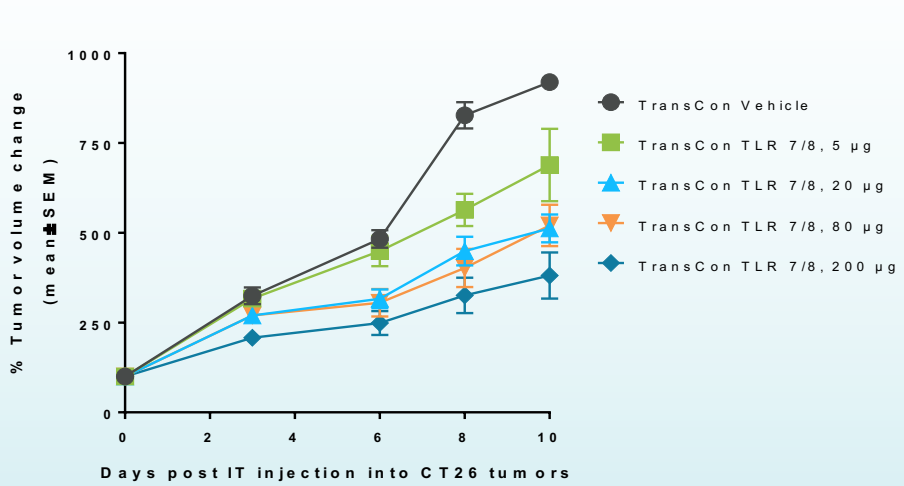
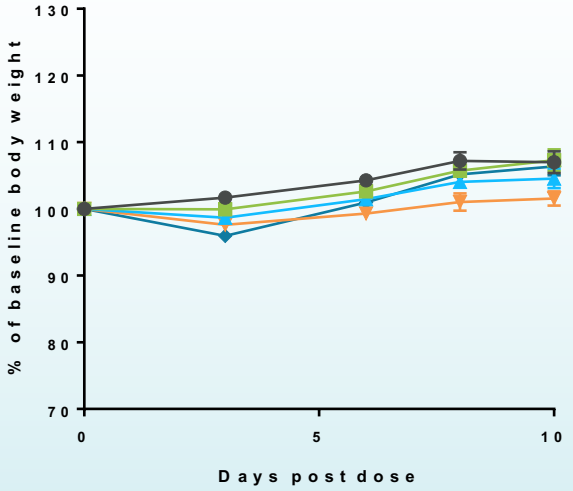
Dose-dependent Tumor Growth Inhibition Following a Single IT Injection of TransCon TLR 7/8 Agonist

Single IT Dosing

Tumor Growth: Dose-dependent Inhibition



Body Weights: All Doses Well Tolerated

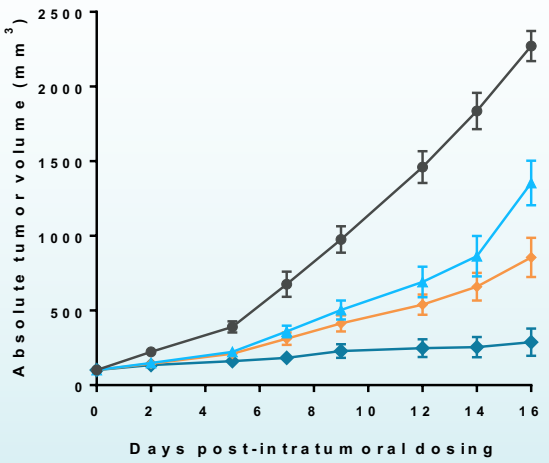


Consistent with MOA, local inflammation and some tumor ulcerations observed

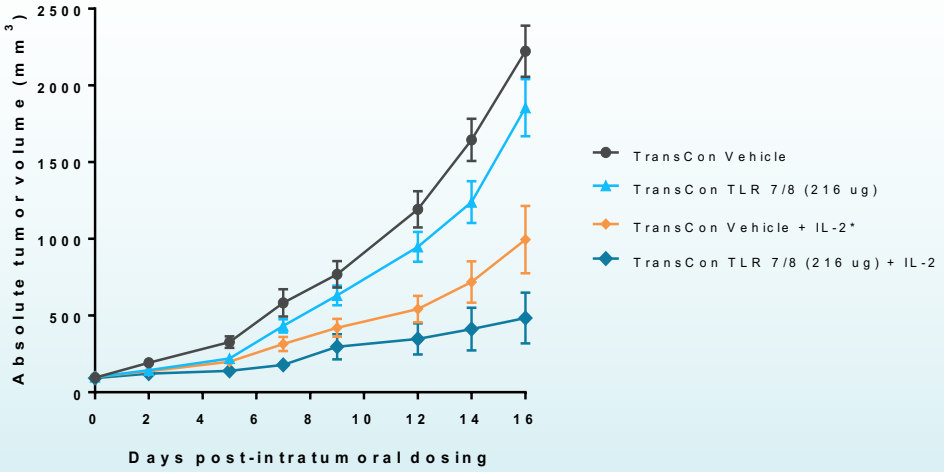
Single-dose of TransCon TLR7/8 Agonist Triggered Abscopal Anti-Tumor Inhibition and Enhanced Anti-tumor Effects of IL-2

Single IT Dosing

Injected Tumor

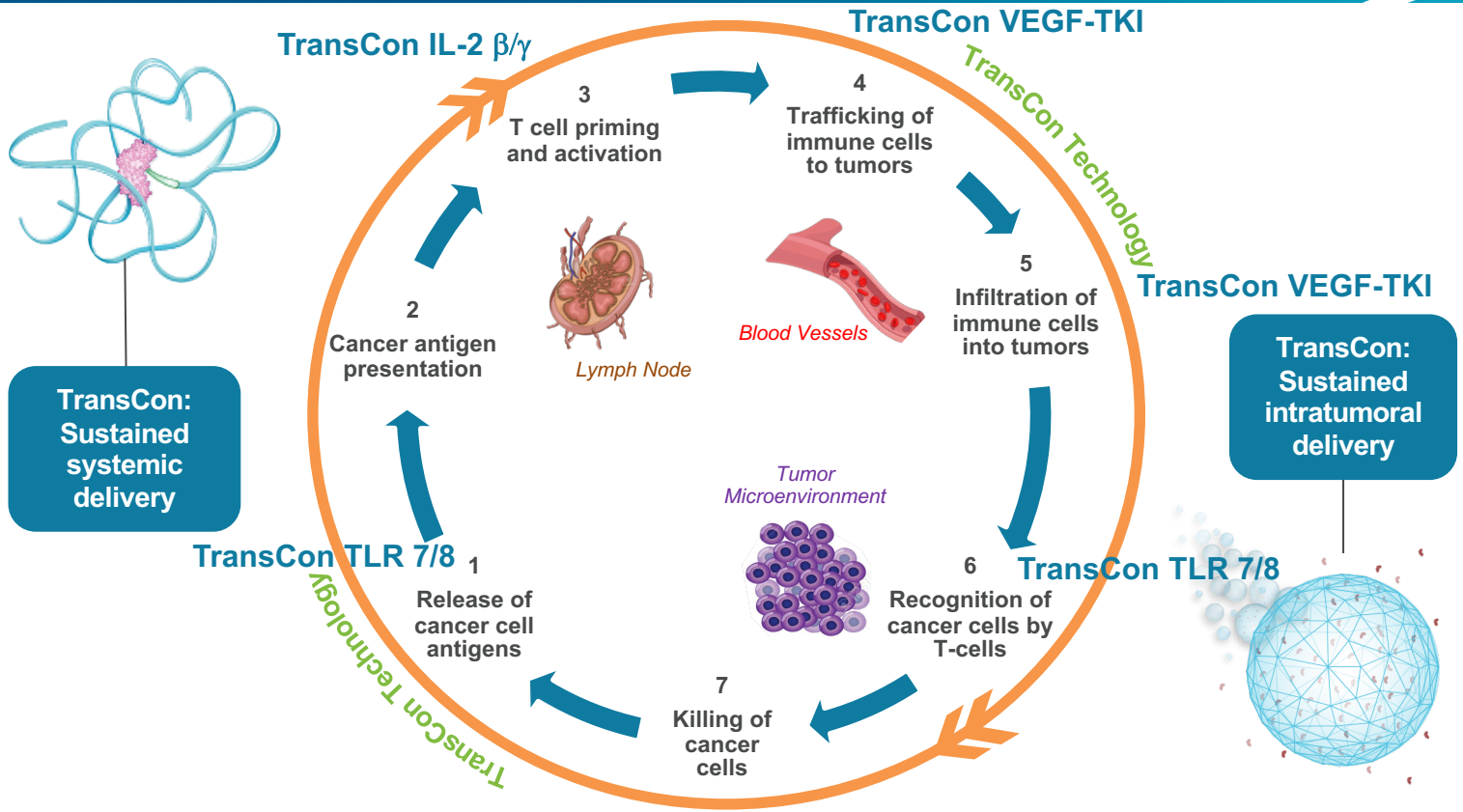


Non-injected Tumor



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

TransCon Immunity Cycle: Seeking a Broad Impact



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

2019 Progress: Expected Milestones