Ascendis Pharma A/S

Investor Presentation

September 2021

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, expectations regarding the potential benefits of SKYTROFA, expectations regarding the projected timing of commercial availability in the U.S. of SKYTROFA, expectations regarding a full suite of patient programs, prospective products, availability of funding, clinical trial results, product approvals and regulatory pathways, collaborations, licensing or other arrangements, the scope, support progress, results and costs of developing our product candidates or any other future product candidates, the potential market size and size of the potential patient populations for SKYTROFA and our product candidates, timing and likelihood of success, plans and objectives of management for future operations, the scope of protection we are able to establish and maintain for intellectual property rights covering our product candidates, future results of current and anticipated products, and the future operations of VISEN Pharmaceuticals, 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 preliminary prospectus supplement related to the proposed public offering and our most recent Annual Report on Form 20-F filed with the SEC on March 10, 2021 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, changed circumstances or otherwise after the date of this presentation.

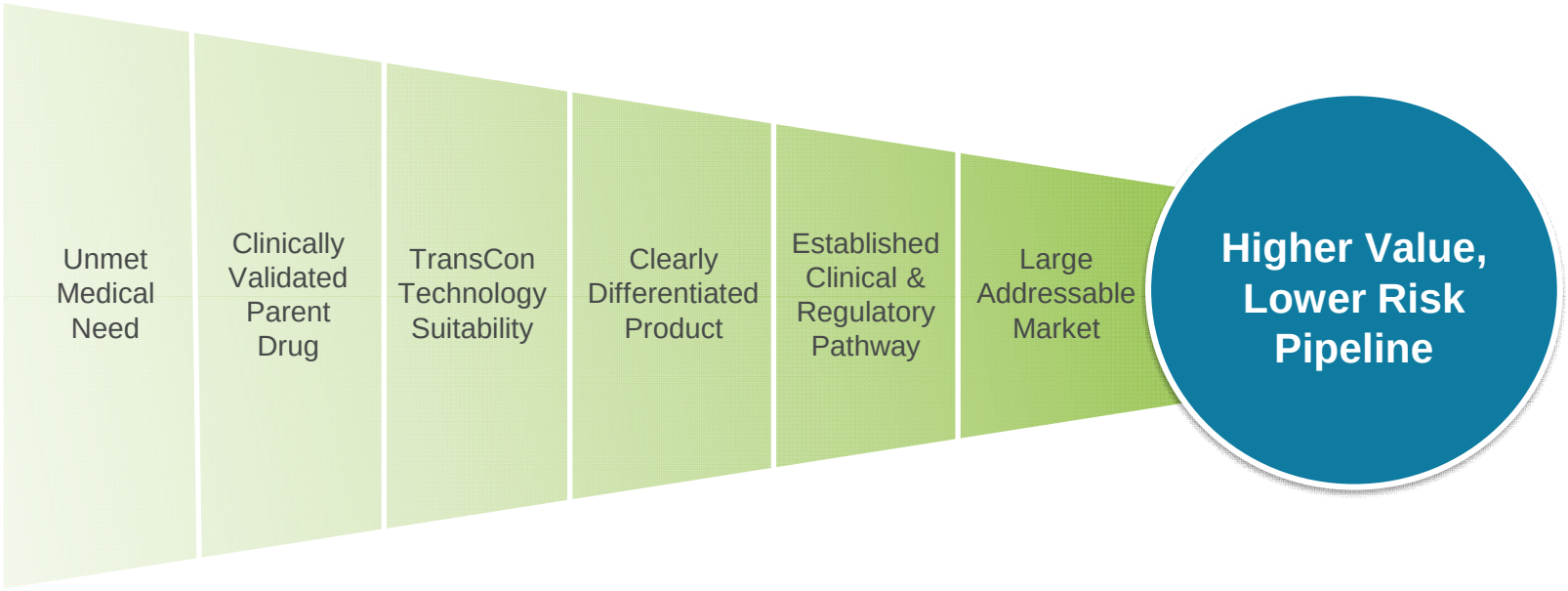
SKYTROFA has been approved by the U.S. Food and Drug Administration for the treatment of pediatric growth hormone deficiency. SKYTROFA is and has been under clinical investigation and has not yet been approved for marketing by the European Medicines Agency or other foreign regulatory authorities. In addition, this presentation concerns other product candidates that are 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.

Company Overview

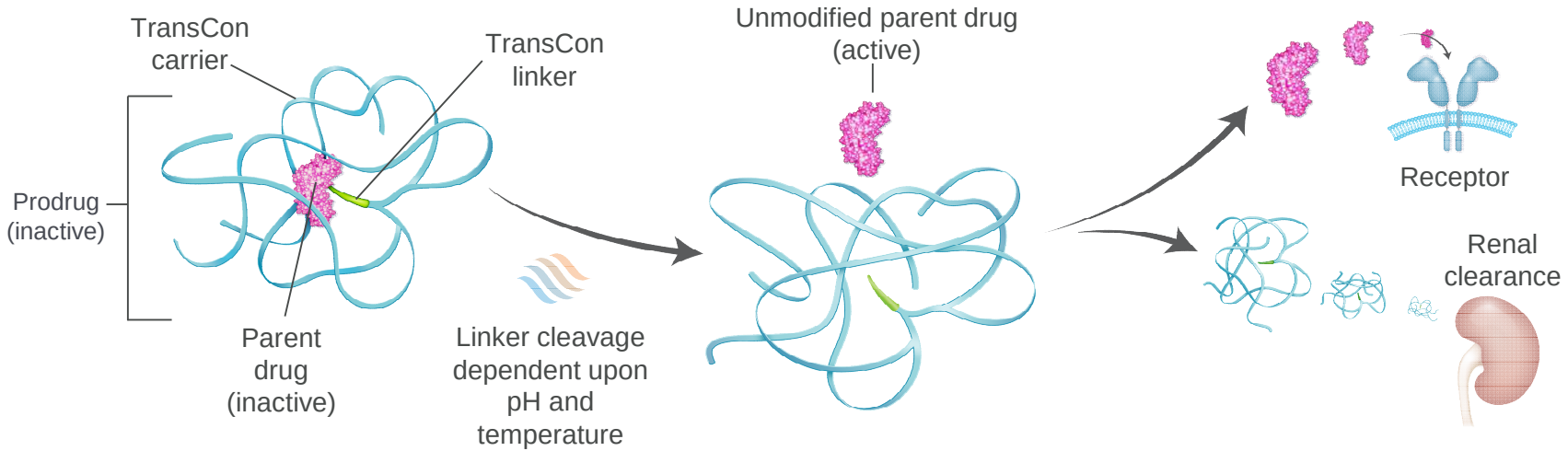
- Create best-in-class products addressing unmet medical needs by applying TransCon™ technologies to parent drugs with clinical proof-of-concept or clinically validated pathways
- Endocrinology rare disease
  - Targeting major areas of unmet need with rare disease market potential combined > $10 billion[1]
  - Three TransCon™ products in development: TransCon hGH, TransCon PTH and TransCon CNP
    - SKYTROFA® (lonapegsomatropin-tcgd) approved in the US by FDA in August 2021 for pediatric growth hormone deficiency (GHD)
    - TransCon hGH currently under EMA review for pediatric GHD
    - Ongoing global[2] phase 3 trials of TransCon PTH and TransCon hGH, and phase 2 trials of TransCon CNP
- Oncology
  - TransCon TLR7/8 Agonist: Phase 1/2 transcendIT-101 Trial
  - TransCon IL-2 β/γ: IND submitted in Q3 2021
- As of June 30, 2021, cash, cash equivalents and marketable securities of €641.3 million

[1] Based on Ascendis Pharma internal estimates
[2] Trials in China being conducted by VISEN Pharmaceuticals.
BLA = Biologics License Application. MAA = Marketing Authorisation Application.

Ascendis Algorithm for Product Innovation



TransCon Technology: Sustained Systemic Release

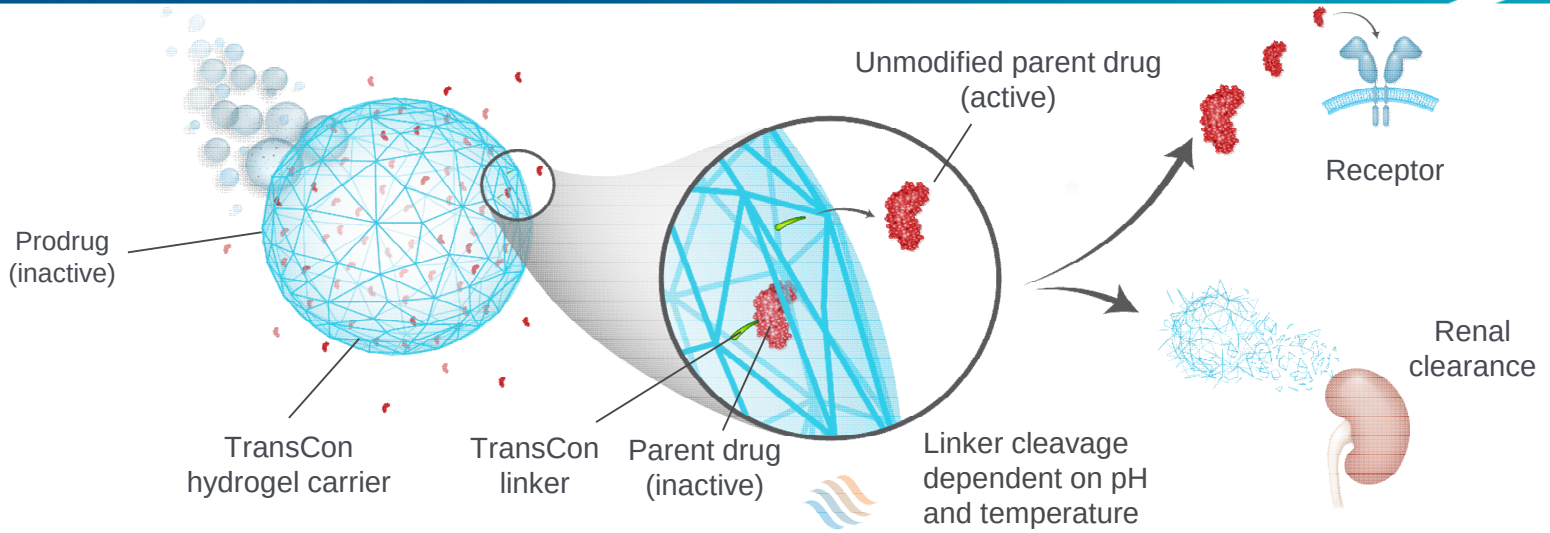


Parent drug is transiently bound to a TransCon linker-soluble carrier moiety, which inactivates and shields parent drug from clearance

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

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

TransCon Technology: Sustained Localized Release

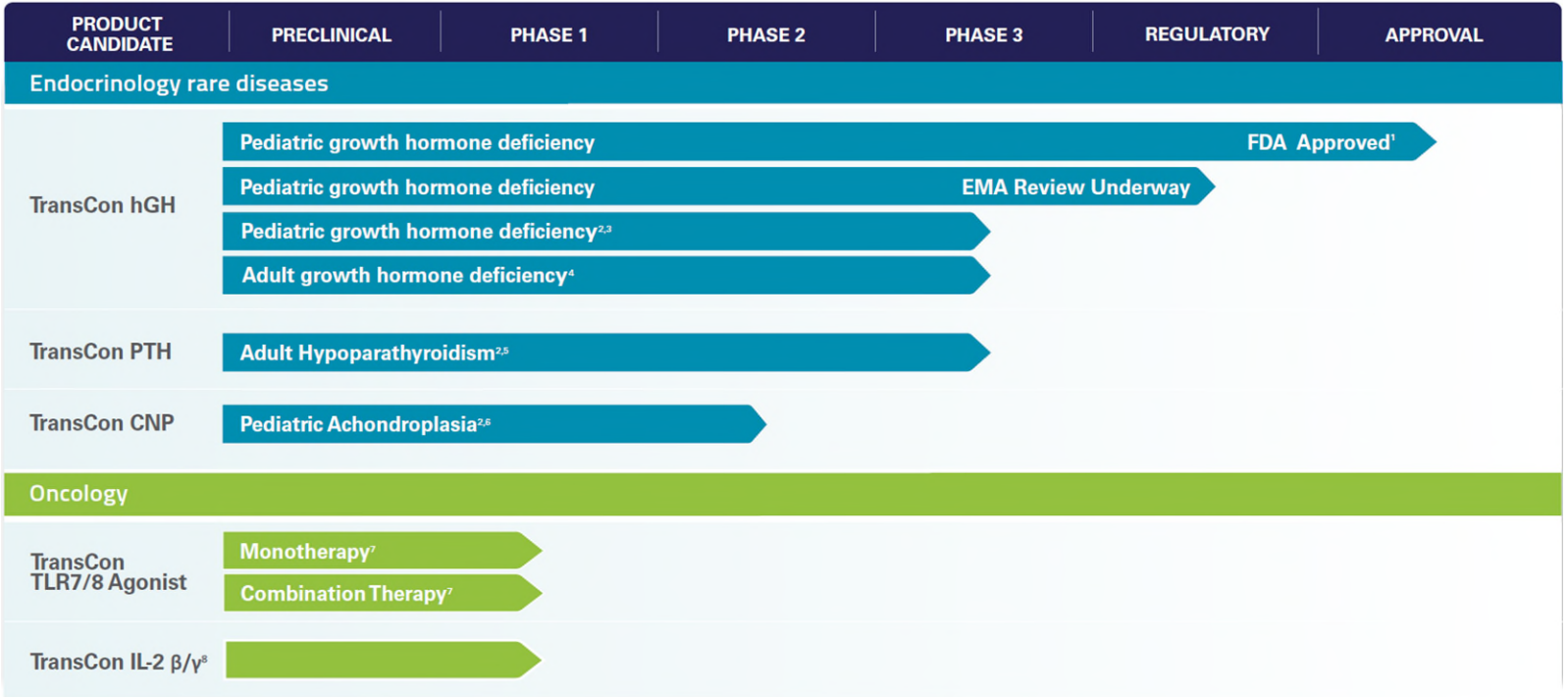


Parent drug is transiently bound to TransCon linker-hydrogel carrier, which inactivates, shields parent drug and prevents clearance

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

Diverse Pipeline of Independent Product Candidates



[1]FDA approved on August 25, 2021.
[2]In development in Greater China through strategic investment in VISEN Pharmaceuticals.
[3]Japanese riGHt Trial.
[4]Global foresiGHt Trial.
[5]North American and European PaTHway Trial, Japanese PaTHway Japan Trial.
[6]North America, Europe, and Oceania ACcomplisH Trial.
[7]transcendIT-101.
[8]IL-βelieγe

Vision 3x3: Building a Leading Global BioPharma Company

Our Goal is to Achieve Sustainable Growth through Multiple Approaches

- Obtain regulatory approval for three independent Endocrinology Rare Disease products
  - TransCon hGH for pediatric growth hormone deficiency
  - TransCon PTH for adult hypoparathyroidism
  - TransCon CNP for achondroplasia
- Grow Endocrinology Rare Disease pipeline through
  - Global clinical reach
  - Pursuing 9 total indications, label optimization, and life cycle management
  - New endocrinology products
- Establish global commercial presence for our Endocrinology Rare Disease area
  - Build integrated commercial organization in North America and select European countries
  - Establish global commercial presence through partners with local expertise and infrastructure
- Advance a high value oncology pipeline with one IND or similar filing each year
- Create a third independent therapeutic area with a diversified pipeline

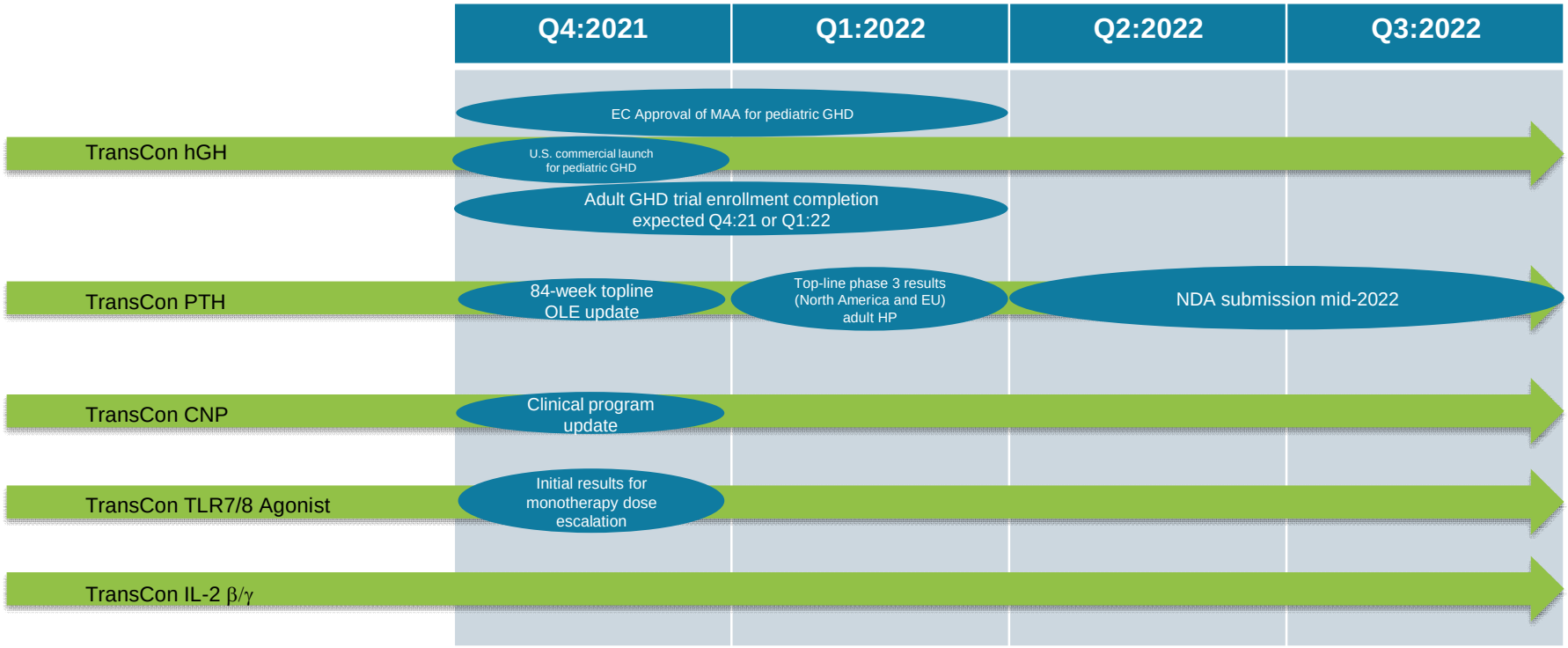
Global Commercial Strategy – Multiple Approaches

- Establishing global commercial presence to deliver potential best-in-class TransCon product candidates to address patients' unmet medical needs
- Laying groundwork for successful future endocrinology rare disease launches
- US commercial organization in place for planned launch of SKYTROFA® in pediatric GHD
- Preparing for potential commercialization in Europe
  - Building integrated organization in select countries for potential TransCon hGH MAA approval in Q4 2021
  - Evaluating established distribution channels in other countries
- Establishing global commercial presence through partners with local expertise and infrastructure
  - Collaborating with VISEN Pharmaceuticals for Greater China
  - Partner in Japan and South Korea when appropriate
  - Serve patients in ROW through established sales and distribution systems

VISEN Pharmaceuticals

- VISEN was formed in 2018 to develop, manufacture, and commercialize TransCon endocrinology rare disease product candidates in Greater China, the second largest pharmaceutical market
  - VISEN responsible for development, manufacturing and commercialization in Greater China
  - Supports integration of Ascendis global clinical development and commercialization strategies
  - VISEN closed Series B equity financing on January 8, 2021; Raised a total of $150 million from new and existing investors
    - Ascendis participated with a $12.5 million investment; retained ~44% of issued and outstanding shares following Series B
- VISEN Announced TransCon R&D Pipeline
  - TransCon hGH: Phase 3 registration clinical trial achieved target enrollment of 150 Chinese children with GHD in March 2021
  - TransCon PTH: Obtained Investigational New Drug (IND) approval for the phase 3 PaTHway China Trial in June 2021 to assess the potential of TransCon PTH as a hormone replacement therapy in subjects with adult hypoparathyroidism
  - TransCon CNP: Received IND approval to initiate phase 2 ACcomplisH China Trial of TransCon CNP for pediatric subjects with achondroplasia

Disclosed Anticipated Milestones in H2:21 and Beyond



Endocrinology Rare Disease

TransCon hGH: Once-Weekly Replacement Therapy

SKYTROFA® Now FDA Approved

Once-weekly

Skytrofa®

lonapegsomatropin-tcgd

- First FDA-approved once-weekly product for pediatric growth hormone deficiency (GHD)
- First FDA-approved product utilizing TransCon™ technology
- In-use room temperature storage for 6 months

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SKYTROFA: Selected Highlights of U.S. Prescribing Information

INDICATIONS AND USAGE	SKYTROFA is a human growth hormone indicated for the treatment of pediatric patients 1 year and older who weigh at least 11.5 kg and have growth failure due to inadequate secretion of endogenous growth hormone (GH)
DOSAGE AND ADMINISTRATION	SKYTROFA should be administered subcutaneously into the abdomen, buttock, or thigh with regular rotation of the injection sites. The recommended dose is 0.24 mg/kg body weight once-weekly. See Full Prescribing Information for instructions on preparation and administration of drug
CONTRAINDICATIONS	• **Acute critical illness** after open heart surgery, abdominal surgery or multiple accidental trauma, or those with acute respiratory failure due to the risk of increased mortality with use of pharmacologic doses of somatropin • **Hypersensitivity** to somatropin or any of the excipients in SKYTROFA • **Children with closed epiphyses** • **Active malignancy** • Active proliferative or severe non-proliferative **diabetic retinopathy** • **Prader-Willi syndrome** who are severely obese, have a history of upper airway obstruction or sleep apnea or have severe respiratory impairment due to the risk of sudden death
ADVERSE REACTIONS	Most common adverse reactions (≥5%) in a clinical trial were viral infection (15%), pyrexia (15%), cough (11%), nausea and vomiting (11%), hemorrhage (7%), diarrhea (6%), abdominal pain (6%), and arthralgia and arthritis (6%).

Reference: SKYTROFA® (lonapegsomatropin-tcgd) prescribing information, Ascendis Pharma

To report SUSPECTED ADVERSE REACTIONS, contact Ascendis Pharma, Inc., at 1-844-442-7236 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Comprehensive Clinical Program

height TRIAL

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

fliGHt TRIAL

Provides data for **switching** patients from daily GH regimens to once-weekly TransCon hGH

enlIGHten TRIAL

Ongoing study for **long-term** safety assessments

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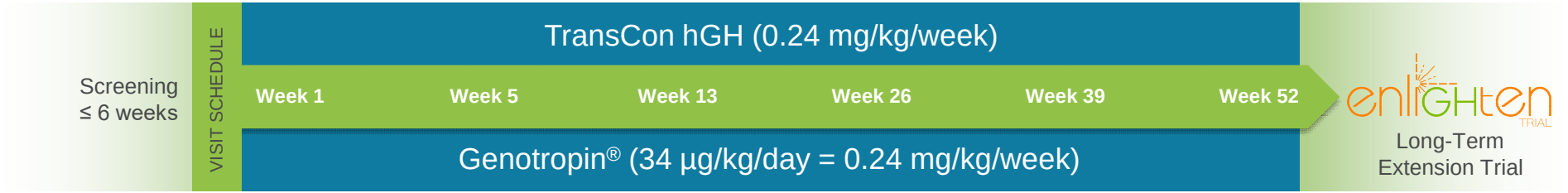
Phase 3 heiGHt Trial

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)

Thornton PS, J Clin Endocrinol Metab, 2021. In press, https://doi.org/10.1210/clinem/dgab529.

SKYTROFA Met Primary Objective of Non-inferiority and Demonstrated Higher AHV at Week 52

	TransCon hGH (n = 105)	Genotropin (n = 56)	Estimate of Treatment Difference
LS Mean AHV at Week 52 (cm/year)	11.2	10.3	0.86
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.
Thornton PS, et al. , J Clini Endocrinol Metabol, 2021;, dgab529.
Thornton P, et al. Oral presentation at ENDO 2019

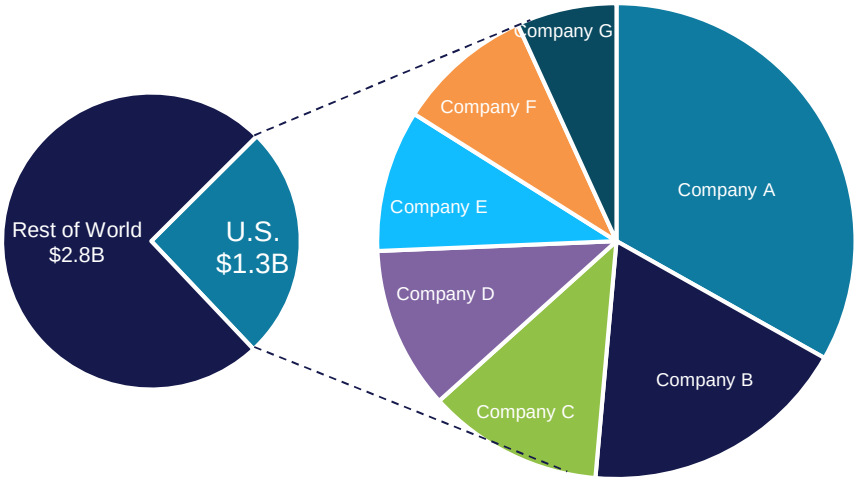
Summary of Adverse Events: Safety Population

	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

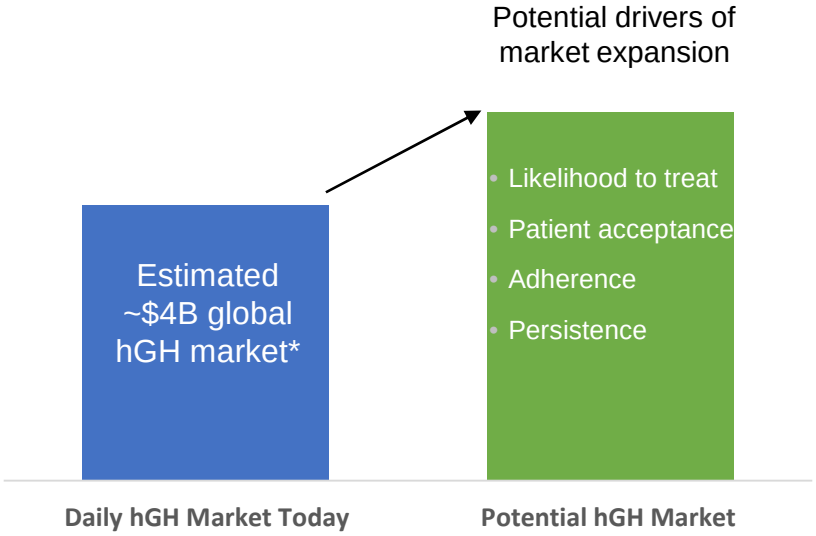
- Adverse events for TransCon hGH similar to type and frequency observed with Genotropin
- No serious adverse events related to study drug in either arm
- No treatment-emergent adverse event led to discontinuation of study drug in either arm

Thornton PS, et al. , J Clini Endocrinol Metabol, 2021;, dgab529.
Data on file, Ascendis Pharma.

Global Human Growth Hormone (hGH) Market Dynamics

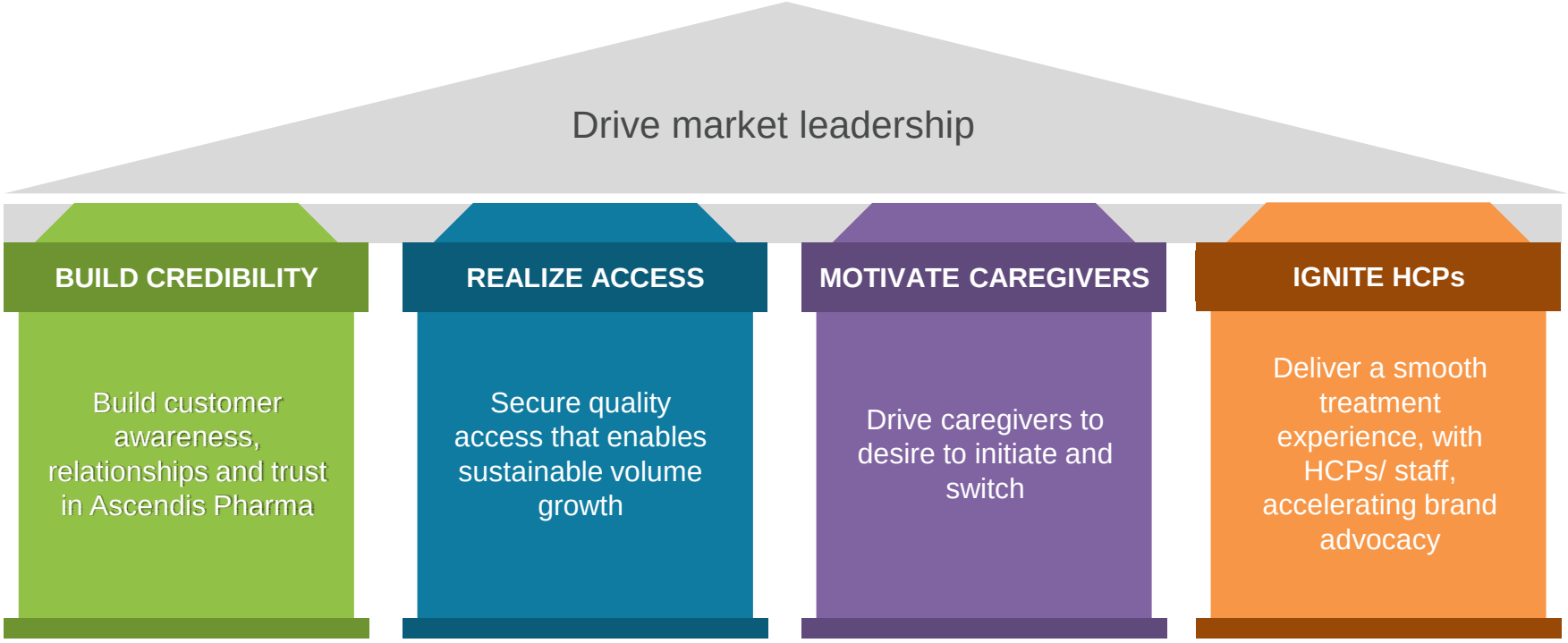


- Global hGH market estimated at ~$4 billion*
- U.S. hGH market estimated at $1.3B* for all indications
  - Pediatric GHD estimated ~$700 million

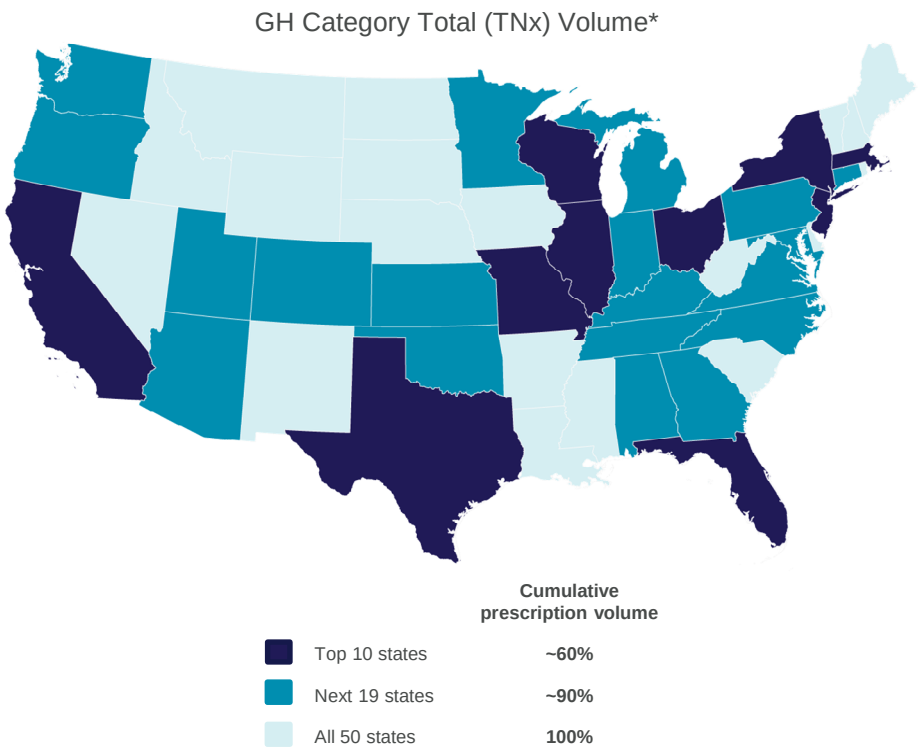


* Ascendis Pharma 2020 market estimate

Our First U.S. Commercial Launch is Expected to Pave the Way for Future Success



Targeting Top Pediatric Endocrinology Markets in the U.S.



National commercial organization planned to cover an expected ~1,400 GH prescribers

- Fully staffed/trained endocrine sales team planned at product launch
- Concentrated market: In the U.S. ~20% of prescribers cover ~80% of volume

* 2019 IQVIA Xponent data

Ascendis Signature Access Program (A·S·A·P) for U.S. Market

PATIENT ENROLLMENT
- Assigned nurse advocate
- Overall case management
- Insurance verification

PATIENT ACTIVATION
- Fast start fulfillment
- Auto-Injector fulfillment
- Starter kit fulfillment
- Nurse training

PATIENT ACCESS
- Benefits verification
- Prior authorization support
- Appeals support
- Out of pocket assistance

Expanding Global Reach and Indications for TransCon hGH

Geographic Expansion for Pediatric GHD

Europe

- MAA approval expected Q4 2021
- Pediatric GHD phase 3 trial in Japan
  - Enrollment ongoing

Greater China* VISEN PHARMA

- Pediatric GHD phase 3 trial in China
  - Target recruitment reached in Q1 2021

Label Expansion

- Global adult GHD phase 3 trial
  - Enrollment ongoing

*Conducted by VISEN Pharmaceuticals.

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TransCon PTH:
PTH Replacement Therapy for Hypoparathyroidism

Hypoparathyroidism

Short-term Symptoms[1]

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

Brain fog

Anxiety due to "fear of crash"

Hypercalcemia
Nocturia, polyuria, constipation, muscle weakness, coma

Patient Burden[2,3]

76%
Either unable to work or report significant interference with work due to HP symptoms

79%
Require hospitalizations or emergency department visits

85%
Report inability to perform household activities

Long-term Complications[4-6]

4-fold
Increased risk of renal disease (nephrocalcinosis, nephrosclerosis, kidney stones & renal insufficiency)

2-fold
Increased risk of depression or bipolar disorder

4-fold
Increased risk of seizures

[1]*Nat Rev Dis Primers* 2017 Aug 31;3:17055 [2]*Qual Life Res* 2021, 30:277–291.
[3]*Endo Pract.* 2014, 20(7);671-679. [4] *J Bone Miner Res* 2013, 28: 2570-2576; [5]*J Clin Endocrinol Metab* 2012, 97(12): 4507-4514. [6]*J Bone Miner Res* 2013, 28: 2277-2285.

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Chronic Hypoparathyroidism: Significant Patient Population

Estimated Prevalence: ~400k in these 5 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

- 2017. Shishiba et. al., Prevalence of postsurgical hypoparathyroidism in Japan: Estimated from the data of multiple institutes
- 1999. Nakamura et. al., Prevalence of Idiopathic Hypoparathyroidism and Pseudohypoparathyroidism in Japan
- Ascendis market research

South Korea

~12k–13k

- S. Korean ICD-10 codes
- Ascendis market research

China

~180k–220k

- 2020, Sui et. al, Time trend analysis of thyroid cancer surgery in China: single institutional database analysis of 15,000 patients
- 2019, Zhao et. al., Features and trends of thyroid cancer in patients with thyroidectomies in Beijing, China between 1994 and 2015: a retrospective study
- World Bank, 2018
- Ascendis market research

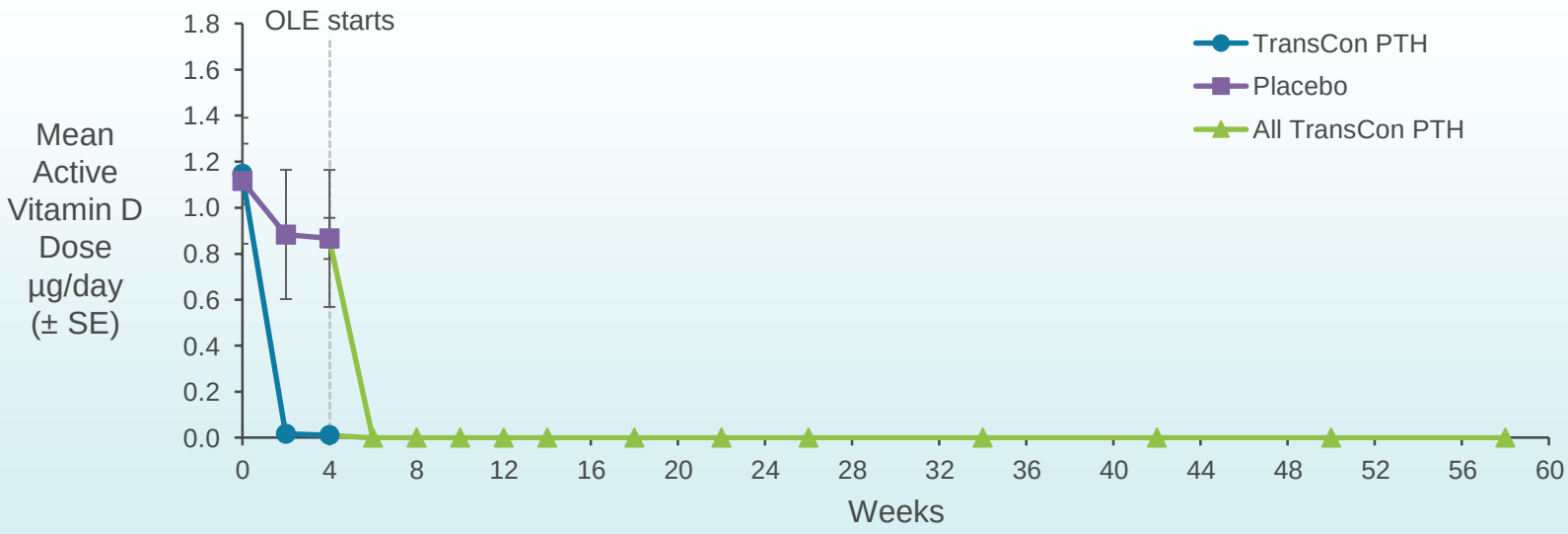
Preliminary PaTH Forward Open-Label Extension (OLE) Data at 58 Weeks

- 58 subjects completed 58 weeks in the open-label extension
- Continued treatment with TransCon PTH demonstrated that:
  - 91% of subjects were off standard of care therapy**
  - Urinary calcium maintained in the normal range
  - Bone markers trended towards the mid-normal levels
  - Quality of life, as measured by SF-36, continued within normal range
- TransCon PTH was well-tolerated at all doses administered
  - No treatment-related serious or severe adverse events occurred, and no treatment-emergent adverse events (TEAEs) led to discontinuation of study drug
  - No change to the safety profile in the OLE portion of the study

Preliminary data support TransCon PTH as a potential hormone replacement therapy for adult HP

Preliminary PaTH Forward OLE week 58 data from live database snapshot. Data on file.
**Not taking active vitamin D and taking ≤600 mg/day of calcium supplements.

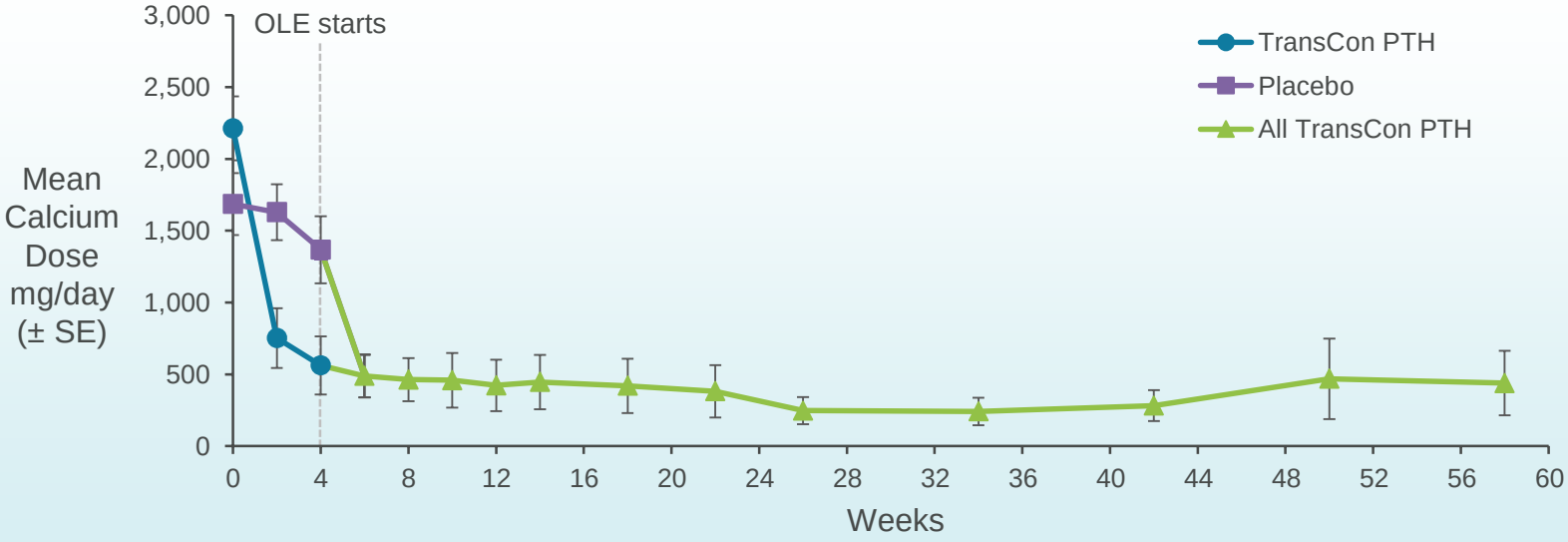
PaTH Forward Mean Active Vitamin D Dose



TransCon PTH enabled discontinuation of active vitamin D within two weeks of treatment initiation

Preliminary PaTH Forward OLE week 58 data from live database snapshot. Data on file.

PaTH Forward Mean Calcium Supplement Dose

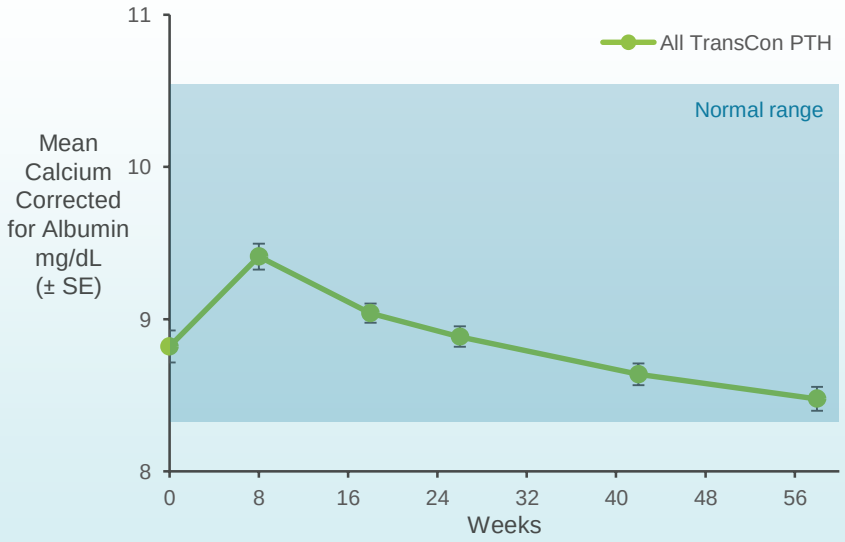


TransCon PTH enabled rapid and sustained calcium supplement reduction;
40 of 58 subjects were taking 0 mg, and 53 of 58 subjects were taking 0 to 600 mg at week 58

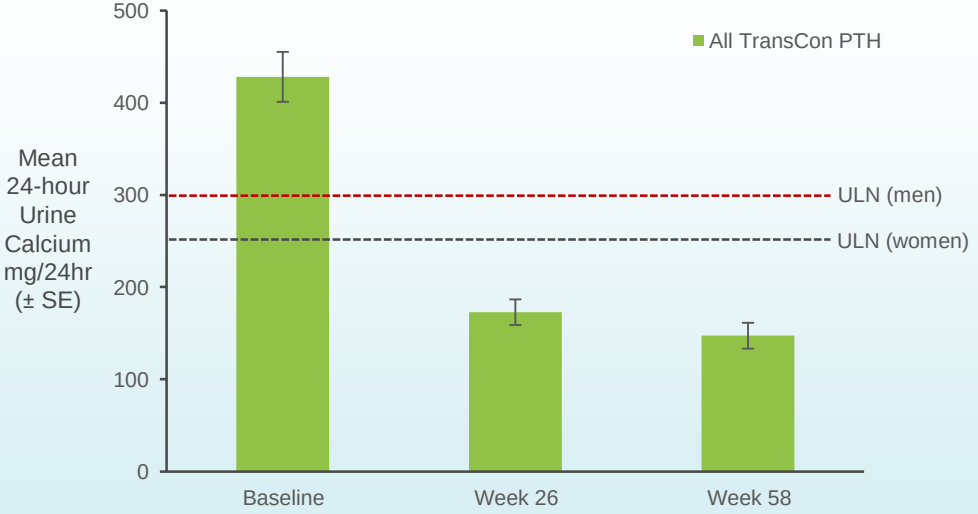
Preliminary PaTH Forward OLE week 58 data from live database snapshot. Data on file.

PaTH Forward Mean Serum Calcium and Mean 24-Hour Urine Calcium

Mean Serum Calcium



Mean 24-hour Urine Calcium



Mean 24-hour urine calcium normalized while maintaining normal mean serum calcium

Preliminary PaTH Forward OLE week 58 data from live database snapshot. Data on file.
ULN = Upper limit of normal.

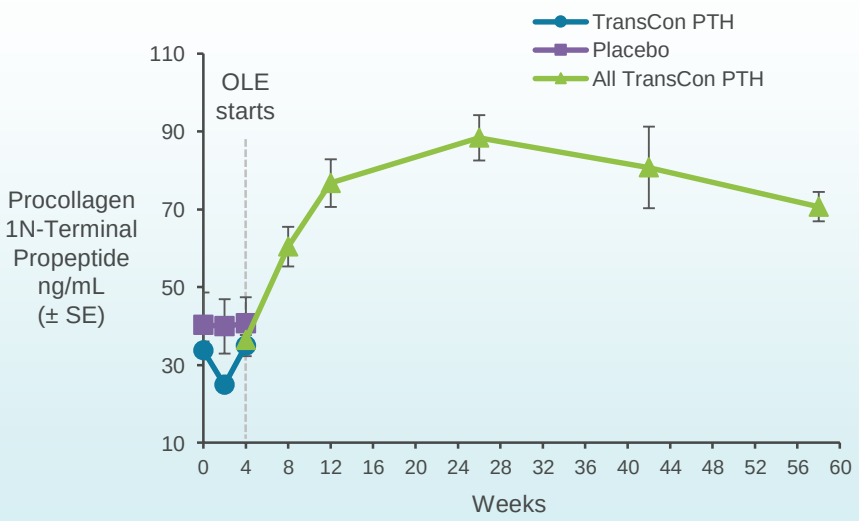
PaTH Forward SF-36® Health Survey Domain Mean Scores (SD)

	All TransCon PTH (N = 59)		
SF-36 Domain	**Baseline**	**Week 26**	**Week 58**
Physical Function	46 (10)	51 (6)	51 (6)
Role Physical	42 (10)	50 (7)	50 (8)
Bodily Pain	45 (10)	50 (9)	50 (8)
General Health	43 (10)	51 (8)	51 (9)
Vitality	43 (11)	53 (8)	51 (10)
Social Functioning	43 (10)	52 (6)	52 (7)
Role Emotional	43 (13)	50 (7)	49 (8)
Mental Health	46 (9)	52 (7)	50 (9)
Physical Component Summary	**44 (11)**	**50 (8)**	**51 (8)**
Mental Component Summary	**44 (11)**	**52 (8)**	**50 (9)**

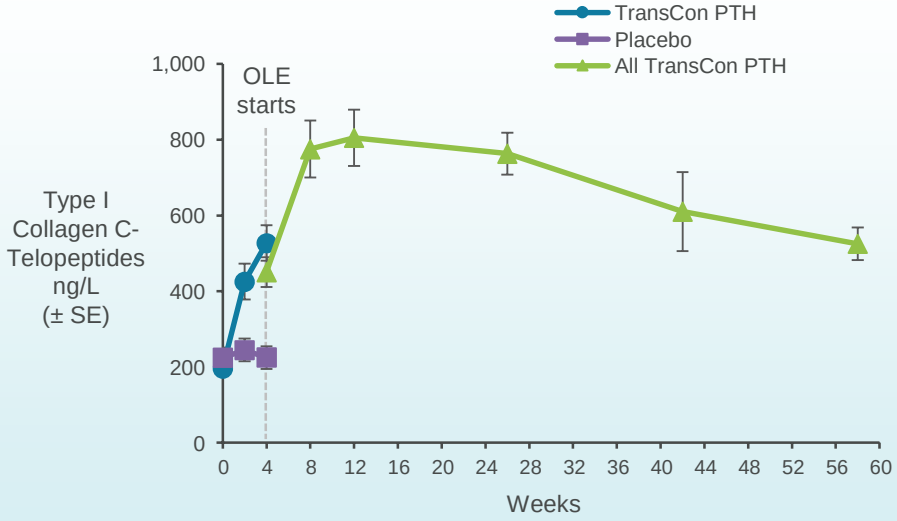
Preliminary PaTH Forward OLE week 58 data from live database snapshot. Data on file.
Green: Means above lower limit of population norm (47)

PaTH Forward P1NP and CTx Bone Markers

Mean P1NP



Mean CTx



TransCon PTH treatment initially increased the levels of anabolic and catabolic bone markers which were trending to mid-normal levels at 58 weeks

Preliminary PaTH Forward OLE week 58 data from live database snapshot. Data on file.

Bone Mineral Density by DXA (Central Lab Reading)
Data from PaTH Forward Subjects with Available DXA Scans

Anatomic region		Group A[1] – Week 26			Group B[1] – Week 58		
		Z-score, mean			Z-score, mean		
		Baseline	Week 26	Change from baseline	Baseline	Week 58	Change from baseline
Lumbar spine L1-L4[2]	n = 42	1.6	1.0	–0.6	1.6	0.9	–0.7
Femoral neck[2]	n = 43	1.0	0.5	–0.5	1.0	0.5	–0.6
Total hip[2]	n = 43	1.0	0.6	–0.4	1.0	0.5	–0.5
Forearm/ 1/3 radius[3]	n = 41	0.3	0.3	0.1	0.3	0.3	0.0

BMD mean Z-scores trended toward normalization and stabilization over 58 weeks in PaTH Forward

[1] Groups A and B included all subjects who had both Week 26 and matching baseline, and Week 58 and matching baseline scans, respectively, read by the central lab.
[2]One subject in Group A was not in Group B, and one subject in Group B was not in Group A.
[3]Two subjects in Group A were not in Group B, and two subjects in Group B were not in Group A.

BMD, bone mineral density. Numbers rounded to the nearest tenth.
Data on file, Ascendis Pharma; 2021.

Preliminary PaTH Forward Safety Summary at 58 Weeks

- TransCon PTH was well-tolerated at all doses administered
- 58 out of 59 randomized subjects continued on TransCon PTH in OLE*
- No drug-related serious TEAEs were reported
- No TEAEs leading to discontinuation of study drug
- TEAEs with TransCon PTH reflect known PTH pharmacology
- Injections were well-tolerated using pen injector planned for commercial presentation
- No change to the safety profile in the OLE portion of the study

No subjects had TEAEs related to hyper- or hypocalcemia leading to ER/urgent care visit and/or hospitalization

Preliminary PaTH Forward OLE week 58 data from live database snapshot. Data on file.
*As of May 7, 2021.
TEAE = Treatment emergent adverse event

PaTH Forward Overall TEAE Summary

	Up to Week 26 All TransCon PTH (N = 59)	Up to Week 58 All TransCon PTH (N = 59)
Subjects With – n (%)		
Treatment-Emergent Adverse Events (TEAE)	37 (63)	44 (75)
Serious TEAE	2 (3)	3 (5)
Severity		
Severe TEAE	1 (2)	2 (3)
Moderate TEAE	9 (15)	10 (17)
Mild TEAE	27 (46)	32 (54)
Related TEAE*	14 (24)	16 (27)
Serious Related TEAE	0	0
TEAE Related to Hyper- or Hypocalcemia Leading to ER/Urgent Care Visit and/or Hospitalization	0	0
TEAE Leading to Discontinuation of Study Drug	0	0
TEAE Leading to Discontinuation of Trial	0	0
TEAE Leading to Death	0	0

Preliminary PaTH Forward OLE week 58 data from live database snapshot. Data on file.
Percentages are calculated based on the number of subjects in the Safety Population. In the severity categories, subjects are displayed for the highest severity only. An AE is considered a TEAE if it occurred after the first dose of TransCon PTH.
*Headache, hypocalcemia, nausea, dizziness, paresthesia, hypercalcemia and asthenia occurred in two or more subjects.

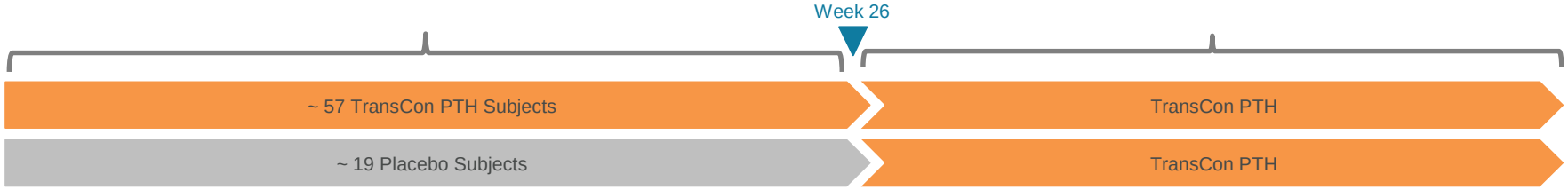
TransCon PTH: A Potential PTH Replacement Therapy

- Preliminary phase 2 PaTH Forward OLE results at 58 weeks*
  - Durable effects of TransCon PTH maintained and was well-tolerated at all doses
  - Subjects appeared to be establishing physiologic calcium metabolism*
    - Bone markers continued to trend towards the mid-normal levels
    - Urine calcium normal
- 58 subjects continue in open-label extension beyond 58 weeks**
  - Further optimization of TransCon PTH dosing being implemented
  - 84-week topline OLE update anticipated in Q4 2021
- Three phase 3 HP trials planned each supporting local regulatory filings
  - North American and European phase 3 PaTHway Trial fully enrolled; topline results expected Q1 2022
  - Japanese phase 3 trial in minimum of 12 HP subjects, PaTHway Japan, initiated
  - Chinese phase 3 trial, PaTHway China, initiated by VISEN Pharmaceuticals in Greater China

*Preliminary PaTH Forward OLE week 58 data from live database snapshot. Data on file.
**As of August 23, 2021.

PaTHway Phase 3 Trial Design

Double-blind, placebo-controlled trial with an open-label extension period
76[1] adults with chronic hypoparathyroidism randomized 3:1 (TransCon PTH:placebo)



Primary Objective
Confirm treatment effect of TransCon PTH in adults with hypoparathyroidism

Key Eligibility Criteria

- Adults with chronic hypoparathyroidism (*i.e.,* for at least 26 weeks)
- Age ≥ 18 years
- Reliant on calcitriol ≥ 0.50 mcg per day or alfacalcidol ≥ 1.0 mcg per day, **and** therapeutic elemental calcium ≥ 800 mg/day
- Serum calcium in normal (or just below normal) range: 7.8–10.6 mg/dL (1.96–2.64 mmol/L)
- No PTH or PTHrP therapy within 4 weeks prior to Screening

Countries Planned

- Europe (Germany, United Kingdom, Denmark, Norway, France, Italy, Hungary)
- North America (United States, Canada)

Primary Composite Endpoint at Week 26

Proportion of subjects with:

- Serum calcium in the normal range (8.3–10.6 mg/dL) ***and***
- Independence from active vitamin D ***and***
- Independence from calcium supplements[2]

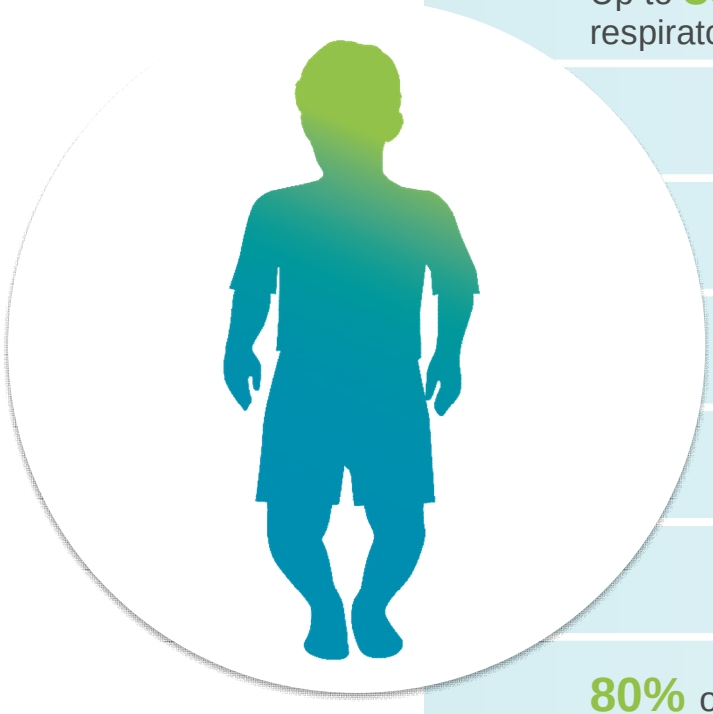
Selected Secondary Endpoints at Week 26

- 24-hour urine calcium excretion
- Serum phosphate levels
- Hypoparathyroidism Patient Experience Scale measures
- 36-Item Short Form Survey (SF-36) measure

[1] Enrollment increased to 76 subjects to ensure evaluable data for 68. Target enrollment achieved in July 2021.
[2] If needed to meet recommended dietary intake of calcium, it is permitted to take calcium supplements ≤ 600 mg/day as a nutritional supplement.

TransCon CNP: Potential New Once-Weekly Growth Treatment Option

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

ascendis pharma

Potential New Once-Weekly Growth Treatment Option

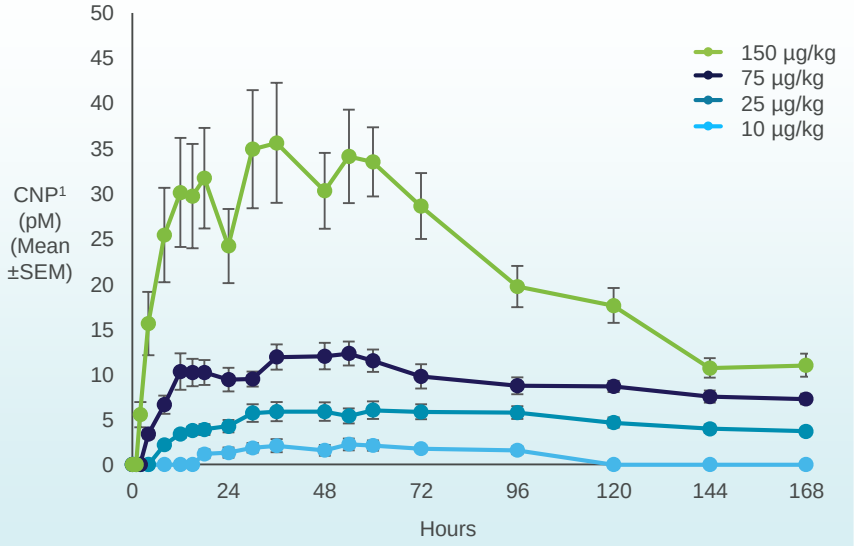
- C-type natriuretic peptide (CNP) is a potential promising therapeutic pathway for treating growth failure and dwarfism
  - Inhibits the overactive signalling resulting from both ligand-dependent and independent signalling through the mutated FGFR3 receptor causing achondroplasia
- Due to its very short 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

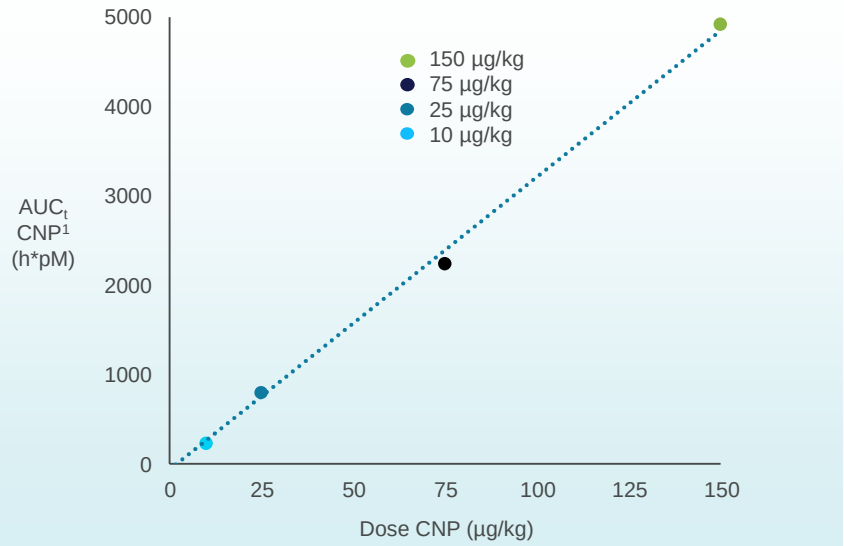
TransCon CNP may provide benefit in several growth disorders — as monotherapy, and potentially in combination with TransCon hGH

Wendt DJ, et al. *J Pharmacol Exp Ther.*. 2015 Apr;353(1):132-49.

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
Ota et al. Oral presentation at ISDS 2019.

TransCon CNP: Safety Profile in Phase 1

- 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

TransCon CNP - Two Randomized Placebo-Controlled Trials

- ACcomplisH Trial
  - Sequential rising dose (6, 20, 50, 100 µg/kg) study in cohorts of 12–15 subjects, double-blind, randomized 3:1 (TransCon CNP to placebo)
  - Higher dose cohorts initiated following blinded DMC review of prior dose 3-month interim data
  - 12-month blinded follow-up with roll over to long-term extension trial
- ACcomplisH China Trial*
  - Designed for dose expansion at effective dose determined from ACcomplisH Trial, double-blind, randomized 3:1 (TransCon CNP to placebo)
  - Plan to enroll over 60 subjects
  - After 12-month blinded period, subjects roll over to long-term extension trial
- TransCon CNP clinical program update expected Q4 2021

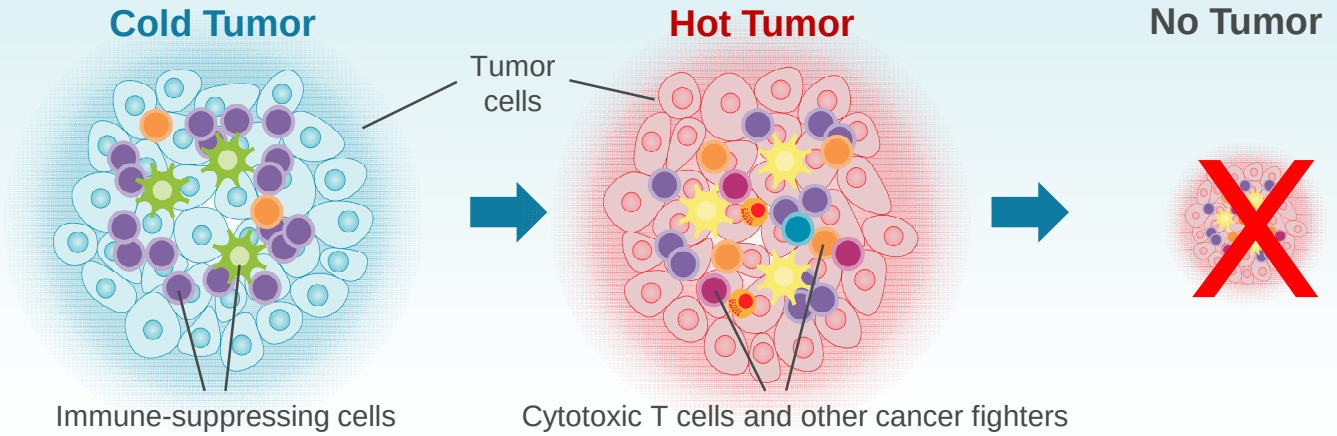
*Conducted by VISEN Pharmaceuticals.

Oncology

TransCon Positioned to Potentially Transform Cancer Therapy

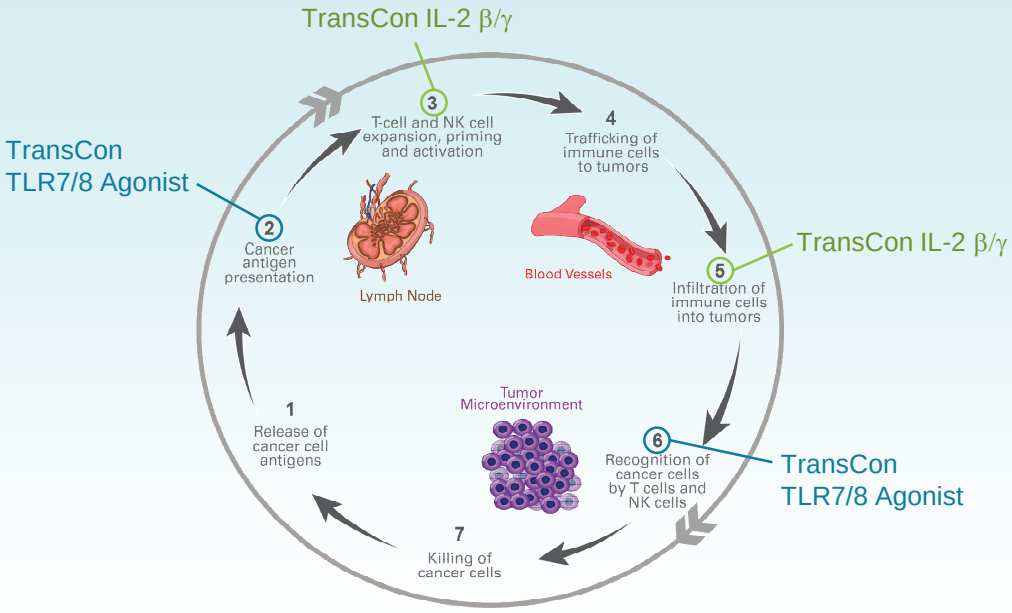
TransCon systemic and intratumoral technologies designed to enhance anti-tumor effects by

- Providing sustained modulation of tumor microenvironments
- Activating cytotoxic immune cells



Applicable to diverse drug classes and mechanisms of action; opportunity for combination approaches

Two Near-term Clinical Candidates – Potential to Address Multiple Steps of the Immunity Cycle



TransCon TLR7/8 Agonist for IT delivery and enhanced tumor-antigen presentation

Designed to enhance antigen presentation and, thereby, promote activation of cytotoxic immune cells (IND submitted)

TransCon IL-2 β/γ for systemic activation of tumor-antigen specific cytotoxic cells

Designed to aid T cell and NK cell expansion and infiltration of immune cells into tumors (IND submitted)

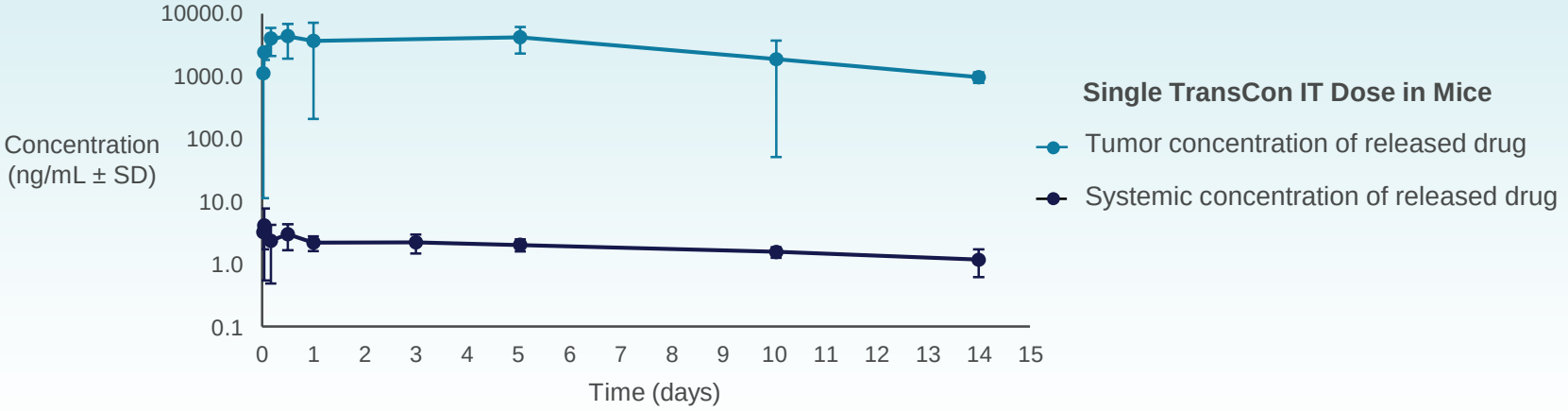
Additional TransCon Candidates

New TransCon candidates with the potential to affect all steps in the immunity cycle

Combination approaches enable impact on all critical steps of anti-tumor response

TransCon IT: Potential Paradigm Shift in Intratumoral Delivery

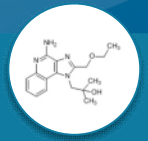
TransCon Intratumoral (IT) designed to address the problems of conventional IT injections including rapid clearance from the tumor, high systemic exposure and toxicity



TransCon IT is designed to stay in the tumor and slowly release the drug ensuring high tumor drug concentration and low systemic exposure

Data on file, Ascendis Pharma.

TransCon TLR7/8 Agonist



TransCon TLR7/8 Agonist

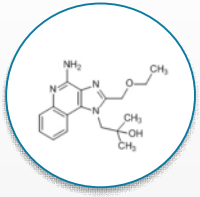
Opportunity for TransCon TLR7/8 Agonist in Solid Tumors

Efficacy
- Each injection designed to provide sustained exposure in the tumor for months to enhance immune activation
- Reduce risk of reaching super-high “ablative”, non-immunogenic levels

Safety
- Low systemic toxicity expected to reduce dose-limiting adverse events
- Infrequent dosing designed to improve practicality and reduce injection-related complications

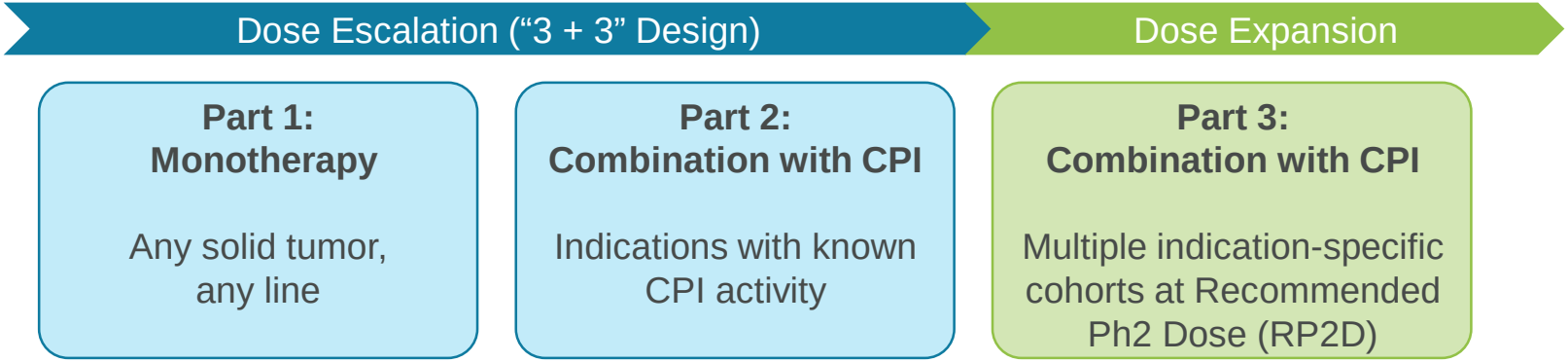
Broad application
- Essentially all solid tumors are accessible for injection

TransCon TLR7/8 Agonist



Designed for ***superior efficacy*** with ***minimal systemic toxicity*** compared to IT injection of parent drug and standard of care

transcendIT-101 Phase 1/2 Trial Design



Objectives:

- Safety and tolerability; define MTD and RP2D
- Pharmacokinetics / pharmacodynamics (PK/PD)
- Preliminary anti-tumor efficacy (ORR, duration of and time to response)

MTD = Maximum Tolerated Dose; ORR = Overall Response Rate using RECIST 1.1.

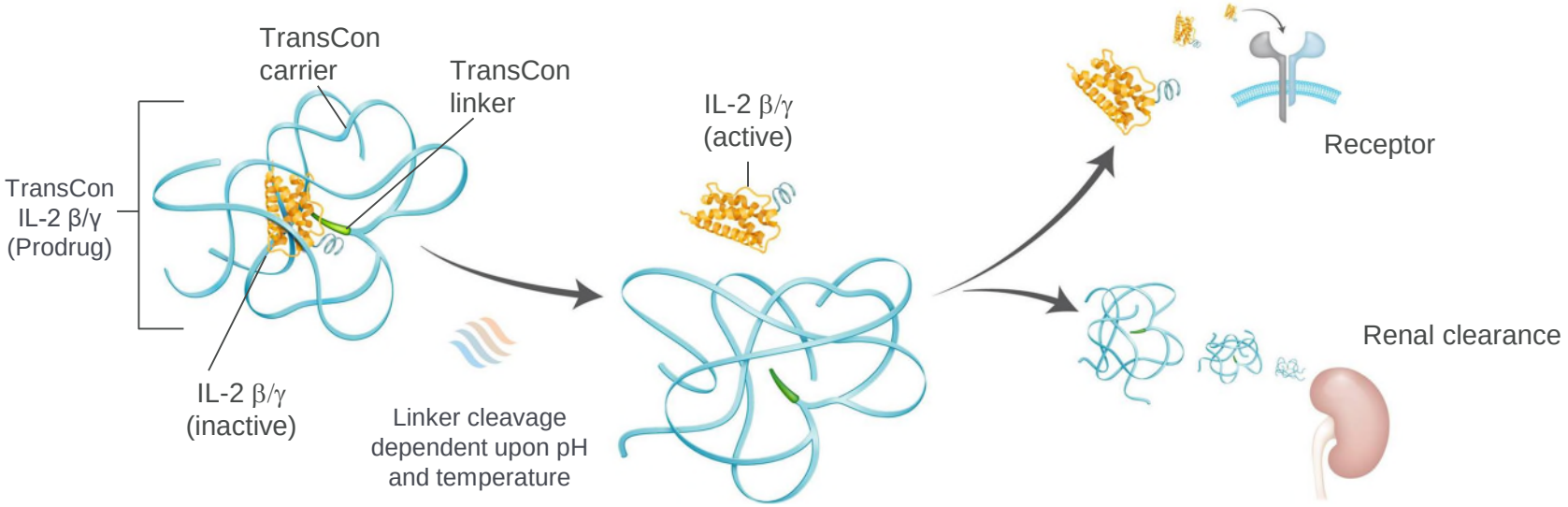
TransCon TLR7/8 Agonist: Aiming to Transform How Cancer is Treated

- TransCon technology offers a new treatment paradigm for IT sustained delivery with potential for superior efficacy and safety
  - Single IT dose provides exposure for weeks/months
  - Low systemic exposure, well tolerated in mice and non-human primates (NHP)
  - Complete tumor regressions, including abscopal effects and immunological memory against re-challenge observed in mouse tumor models
  - Sustained IT release is designed to enable superior efficacy
- transcendIT-101 Trial ongoing
  - Focus on HPV-associated tumors as first indications
  - Initiated CPI combo dose in Q3 2021
  - Initial results for monotherapy dose escalation expected Q4 2021

TransCon IL-2 β/γ

TransCon
IL-2 β/γ

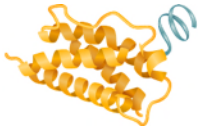
Design of TransCon IL-2 β/γ



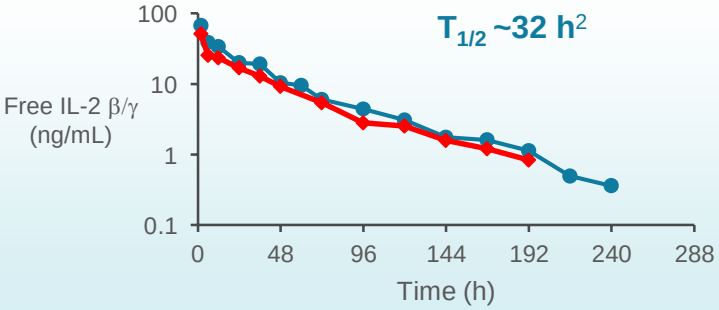
TransCon IL-2 β/γ is designed to provide sustained, long-lasting exposure of a highly-potent, proprietary IL-2 variant using the linker and carrier from TransCon hGH

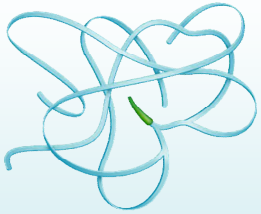
TransCon IL-2 β/γ: Optimized β/γ Bias, Potency and PK

Variant	β/γ Bias	Potency Reduction[1]
IL-2	No	n/a
IL-2 β/γ 5 kDa	Yes	~4-fold
IL-2 β/γ 10 kDa	Yes	~6-fold
IL-2 β/γ 30 kDa	Yes	~20-fold



Optimizing IL-2 β/γ bias and potency through permanent PEGylation





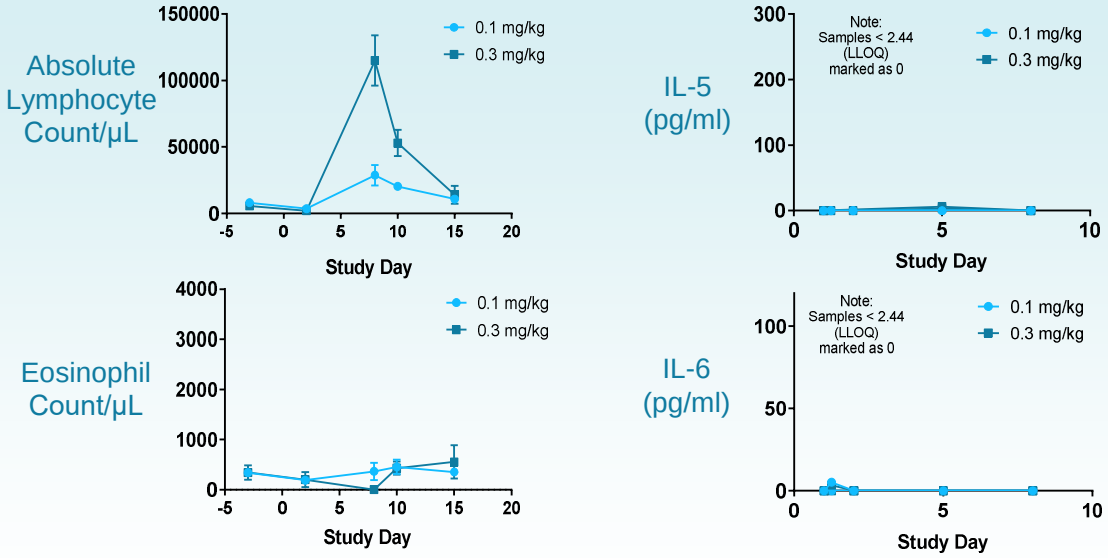
TransCon technology provides low C_{max} and prolonged exposure

Independently optimized receptor bias and potency as well as pharmacokinetics, to create a potentially best-in-class IL-2 product

*Data on file, Ascendis Pharma. [1]Potency determined in HH cell-based assay expressing IL-2R β/γ. [2]NHP Study Dose: 0.1 mg/kg.

Robust Increase in Absolute Lymphocyte Count with Minimal Eosinophil Expansion in NHP

TransCon IL-2 β/γ[1] (Single Dose on Day 1)



Doses are indicated as mg/kg; average animal weight 3.13 kg (2.46 – 3.69 kg)

- Mean ~27-fold increase in Absolute Lymphocyte Count
- Minimal impact on eosinophils
- No capillary leak syndrome observed up to 0.9 mg/kg
- *In vivo* proliferation responses remain dose dependent up to 0.3 mg/kg

Single dose supporting Q3W dosing; minimal effect on eosinophils, minimal IL-5 and IL-6 levels suggests low risk of vascular leak syndrome syndrome[2,3]

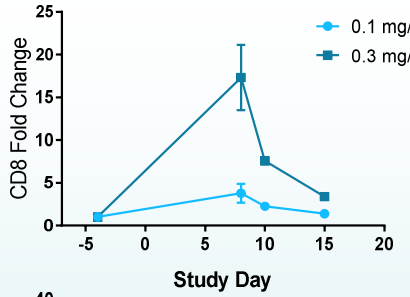
Q3W = every 3 weeks.
[1] Data on file, Ascendis Pharma. [2]Rand, et al. *J Clin Invest.* 1991; 88: 825. [3]Van Haelst Pisani C, et al. *Blood.* 1991;78:1538.

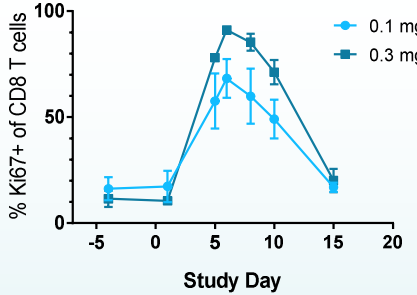
Potent CD8+ T Cell and NK Cell Peripheral Expansion and Activation in NHP

Fold Change*

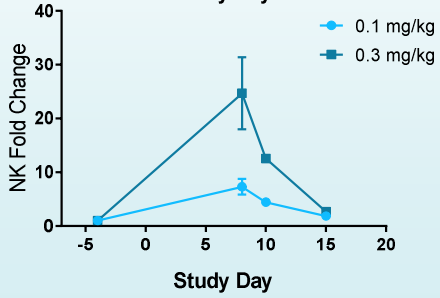
% Ki67+

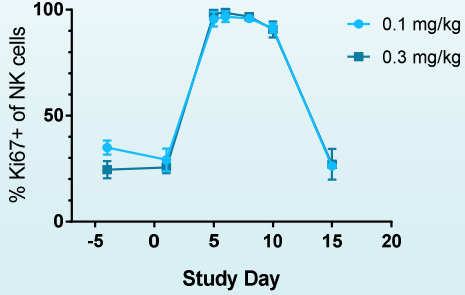
CD8+ T cells





NK cells





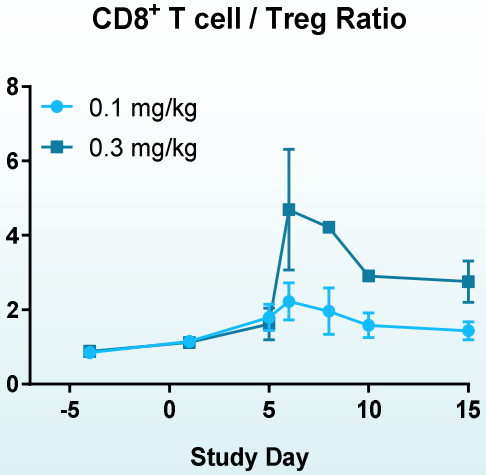
- Mean ~17-fold expansion of CD8+ T cells
- Mean ~25-fold expansion of NK cells
- Almost 100% of cells expressing Ki67 activation marker

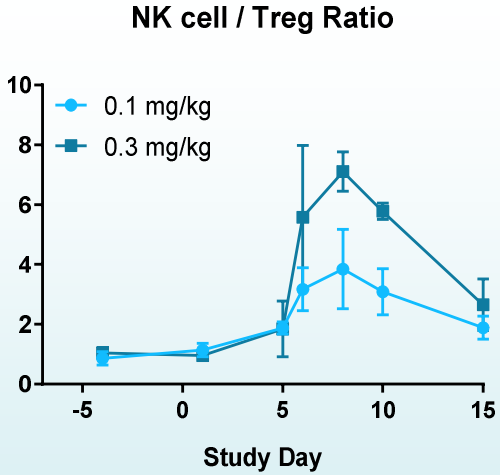
Expansion and activation of cytotoxic lymphocyte subsets observed following a single dose of TransCon IL-2 β/γ

*Fold change using cell counts derived from hematology lymphocyte counts and flow cytometry-based frequencies within lymphocytes.
Data on file, Ascendis Pharma.

TransCon IL-2 β/γ Expands Ratios of CD8+ T Cells and NK Cells Over Treg Cells in NHP

Fold change of cell ratios





- Mean ~5-fold increase of CD8+ T cell / Treg ratio
- Mean ~7-fold expansion of NK cell / Treg ratio

A single dose of TransCon IL-2 β/γ resulted in durable and robust increases in the ratios of CD8+ T cells and NK cells over Treg cells in NHP

Data on file, Ascendis Pharma.

Evaluation of Immune Memory and Potential Cross-immunity Following TransCon IL-2 β/γ plus TransCon TLR7/8 Agonist

Syngeneic CT26 tumor model (colon-derived tumor line)

Treatment with TransCon IL-2 β/γ + TransCon TLR7/8 Agonist

Re-challenge of complete responders with CT26

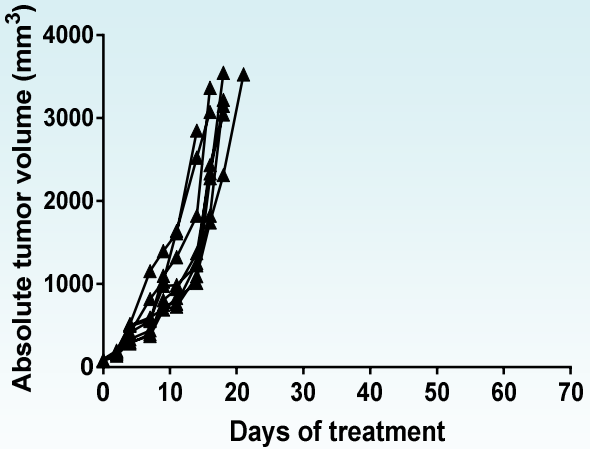
- 73 days after initial treatment
- No additional treatment

Challenge of complete responders with different tumor type, EMT6 (mammary-derived)

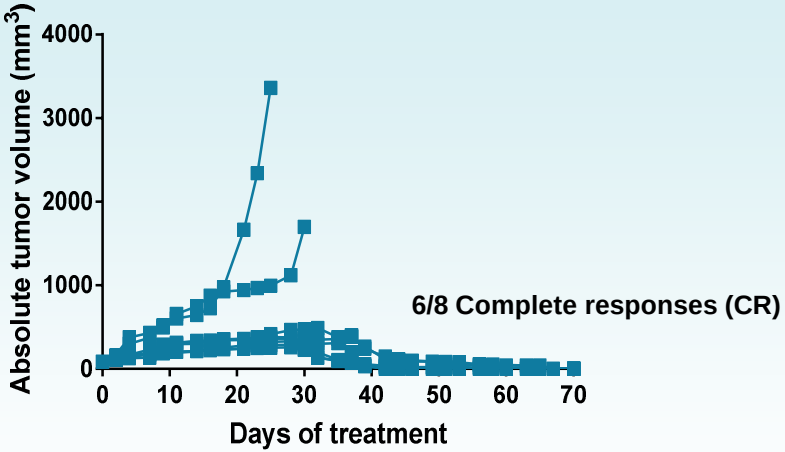
- 28 days after CT26 re-challenge
- No additional treatment

TransCon IL-2 β/γ Plus TransCon TLR7/8 Agonist Resulted in Durable Complete Tumor Regressions in the CT26 Tumor Model

Buffer control



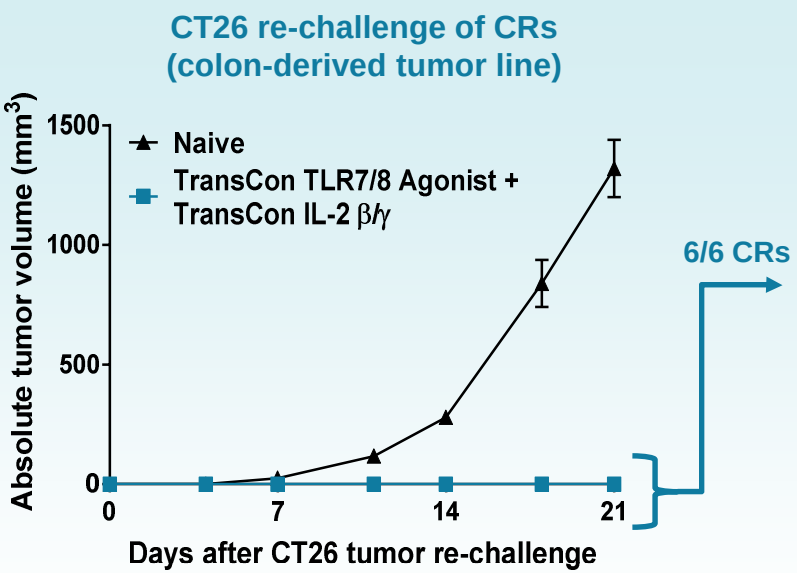
TransCon IL-2 β/γ (3 doses) + TransCon TLR7/8 Agonist (single dose)

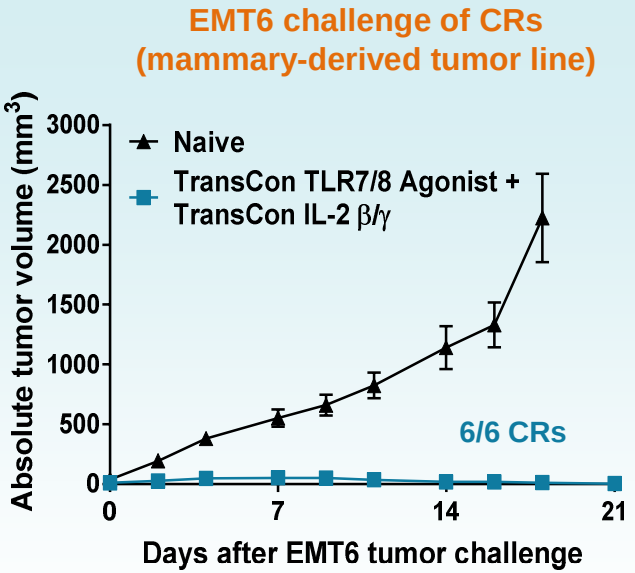


The immune activating mechanism of action of TransCon IL-2 β/γ plus TransCon TLR7/8 Agonist and complete responses suggests potential for anti-tumor immune memory

Data on file, Ascendis Pharma.

Potent Immune Memory and Cross-Reactive Anti-Tumor Response Against a New Tumor Type





Protection against initial tumor and a new tumor type, suggesting potent anti-tumor memory and cross-reactive anti-tumor immunity

Data on file, Ascendis Pharma.

Potential Paradigm Shift in How Cancer is Treated

- Building a pipeline using TransCon technologies that may enable a new treatment paradigm building upon well-known biology
- Two product candidates demonstrating potentially best-in-class properties
  - TransCon TLR7/8 Agonist designed for IT, long-term sustained release for robust efficacy with minimal systemic adverse events; transcendIT-101 Trial ongoing
    - Focus on HPV-associated tumors as first indications
    - Initiated CPI combo dose escalation in Q3 2021
    - Initial results for monotherapy dose escalation expected Q4 2021
  - TransCon IL-2 β/γ designed for optimized IL-2Rβ/γ bias and potency, combined with low C_{max} and long exposure; IND planned for Q3 submitted September 2021
  - Combination resulted in potent anti-tumor responses and immunological memory, including cross-immunity against a new tumor type

Thank you

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(650) 374-6343