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

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**FORM 6-K**

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

For the month of January, 2021

Commission File Number: 001-36815

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**Ascendis Pharma A/S**

(Exact Name of Registrant as Specified in Its Charter)

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

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

Form 20-F       Form 40-F

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

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

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Spokespersons of Ascendis Pharma A/S (the “Company”) plan to present the information in the presentation slides attached hereto as Exhibit 99.1 at various investor and analyst meetings scheduled during the week of January 11, 2021. In addition, furnished hereto as Exhibit 99.2 is a press release of the Company dated January 10, 2021.

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

**Exhibits**

99.1 [Company Presentation](#)

99.2 [Press Release](#)

**SIGNATURES**

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

**Ascendis Pharma A/S**

Date: January 11, 2021

By: /s/ Michael Wolff Jensen

Michael Wolff Jensen

Chairman and Senior Vice President, Chief Legal Officer



# Ascendis Pharma A/S

39th Annual J.P. Morgan Healthcare Conference  
January 11, 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, prospective products, availability of funding, clinical trial results, product approvals and regulatory pathways, collaborations, licensing or other arrangements, the scope, 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 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 most recent Annual Report on Form 20-F filed with the SEC on April 3, 2020 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.

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.

# 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
  - TransCon hGH:
    - Pediatric growth hormone deficiency (GHD): BLA and MAA submitted, phase 3 trials in China<sup>1</sup> ongoing and Japan initiated
    - Adult GHD: Global phase 3 foresiGHt Trial ongoing
  - TransCon PTH: Adult hypoparathyroidism (HP) phase 3 PaTHway Trial in North America and Europe ongoing
  - TransCon CNP: Achondroplasia phase 2 trials: ACcomplishH Trial ongoing and ACcomplishH China Trial<sup>1</sup> initiated
- Oncology
  - TransCon TLR7/8 Agonist: IND filed
  - TransCon IL-2  $\beta/\gamma$ : IND filing or similar expected in Q3 2021
- As of September 30, 2020, cash, cash equivalents and marketable securities of €957.5 million

3 | <sup>1</sup> Conducted by VISEN Pharmaceuticals.  
BLA = Biologics License Application. MAA = Marketing Authorisation Application.

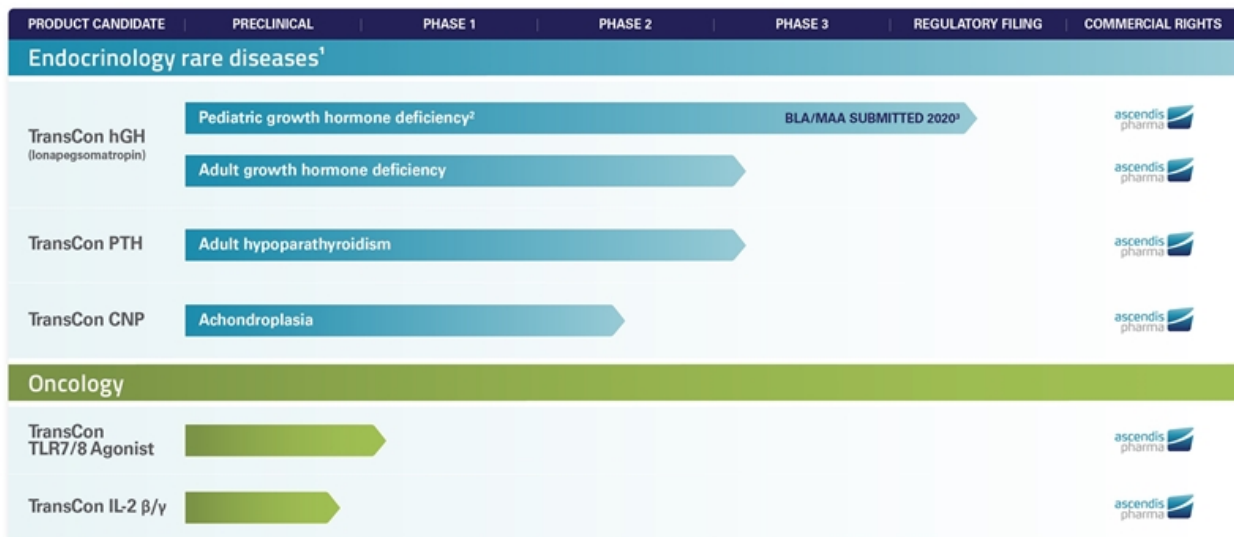
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# Vision 3x3: Building a Leading BioPharma Company

## 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

# Diverse Pipeline of Independent Product Candidates



<sup>1</sup>Excludes rights granted to VISEN Pharmaceuticals in Greater China.

<sup>2</sup>In phase 3 development for pediatric growth hormone deficiency in Greater China through strategic investment in VISEN Pharmaceuticals.

<sup>3</sup>US PDUFA June 25, 2021.

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## Endocrinology Rare Disease



# TransCon hGH: Once-Weekly Replacement Therapy

# Growth Hormone Supports Overall Endocrine Health

## BODY COMPOSITION<sup>2,3,4</sup>



ULTIMATE HEIGHT  
ACHIEVEMENT<sup>1</sup>



## CARDIOVASCULAR DISEASE<sup>6,7</sup>



MENTAL HEALTH<sup>5</sup>



FRACTURES<sup>8</sup>

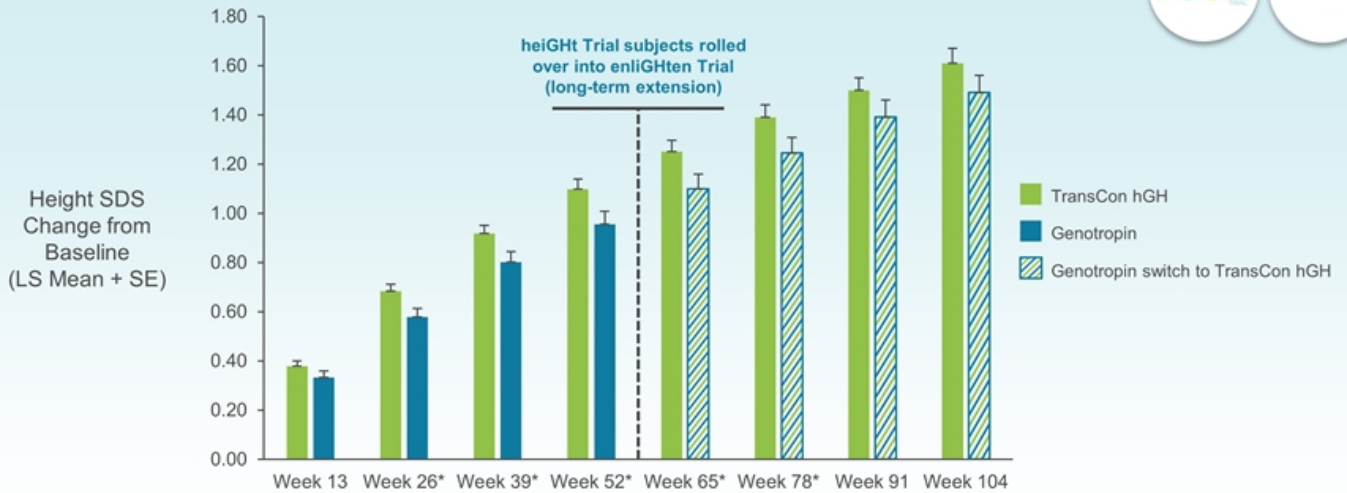
Daily hGH addresses all the symptoms of the disease; long-acting growth hormone products must retain the properties of hGH to adequately address the totality of the disease

<sup>1</sup>de Boer, H. et al. *J. Clin. Endocrinol. Metab.* 1997; 82(7): 2032-2036. <sup>2</sup>Rutherford, O. M. et al. *Clin. Endocrinol* 1991; 34(6): 469-475. <sup>3</sup>Colle, M., J. Auzeber. *Horm. Res.* 1993; 39(5-6): 192-196. <sup>4</sup>Johannsson, G., et al. *J. Clin. Endocrinol. Metab.* 1999; 84(12): 4516-4524. <sup>5</sup>Stabler, B. et al. *Horm. Res.* 1996; 45(1-2) 30-33 <sup>6</sup>Leong, G., Johannsson, G. *Horm. Res.* 2003; 60(suppl1): 78-85 <sup>7</sup>Colao, A. et al. *J. Clin. Endocrinol. Metab.* 2002; 87(8): 3650-3655. <sup>8</sup>Bex, M., Bouillon, R. *Horm. Res.* 2003; 60(suppl3): 80-86.

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# Pediatric GHD Patients Continue Approaching Normal Height



Children initially treated with TransCon hGH maintained an advantage in height SDS improvement

9 | \*Denotes treatment difference resulted in a nominal P value < 0.05. Maniatis A et al. Oral presentation at ENDO 2020 and Data on file.

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# Key Learnings from TransCon hGH Pediatric Clinical Trials

- TransCon hGH demonstrated a safety profile comparable to that of a daily hGH<sup>1</sup>
- TransCon hGH demonstrated superior AHV<sup>2</sup> compared to a daily hGH with a PK profile<sup>2</sup> of released hGH that may lead to more efficient utilization by target tissues
- Data suggest hGH released from TransCon hGH maintains the same mode of action as daily hGH and preserves the biological balance between hGH and IGF-1 effects<sup>1,2,3,4</sup>
  - TransCon hGH and a daily hGH demonstrated similar relationship between change in height SDS and change in average IGF-1 SDS<sup>3,4,5</sup>
  - TransCon hGH showed predictable linear IGF-1 response to dose titrations<sup>5</sup>
- TransCon hGH demonstrated consistent safety and efficacy profile following switch from daily hGH in both fliGHt and enliGHten trials<sup>1</sup>

<sup>1</sup>Maniatis A et al. Oral presentation at ENDO 2020.

<sup>2</sup>Thornton P, et al. Oral presentation at ENDO 2019.

<sup>3</sup>Chatelain P, et al. *J Clin Endocrinol Metab* 2017, 102(5): 1673 – 1682.

<sup>4</sup>Vlachopapadopoulou et al. Oral presentation at ESPE 2019.

<sup>5</sup>Data on file.

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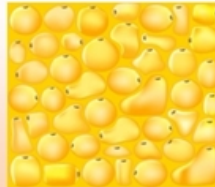
# Impact of Growth Hormone Distribution

TransCon hGH is designed to release hGH to achieve the same tissue distribution and receptor activation in the body as daily hGH, with once-weekly administration



## BONE

Optimal growth achieved  
*via* direct stimulation of GH  
receptors in bone and  
through IGF-1<sup>1</sup>



## ADIPOSE TISSUE

hGH directly stimulates the  
breakdown of fat<sup>1</sup>

11 | <sup>1</sup>Kaplan SA, Cohen P. *J Clin Endocrinol Metab.* 2007;92(12):4529-4535.

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# Adult GHD Global Phase 3 ForesiGHt Trial Design



## Primary Objective: Demonstrate efficacy compared to placebo

### Endpoints

- **Primary:** Change from baseline in trunk % fat at 38 weeks
- **Secondary:** Change from baseline in trunk fat mass (kg) and total body lean mass (kg) at 38 weeks
- **Exploratory:** Total body fat mass, trunk lean mass, visceral adipose tissue, total body bone mineral content and density, TRIM-AGHD, PGIS, and EQ-5D-5L scores
- **Safety:** AEs, labs, vital signs, anti-drug antibodies, ECGs, fundoscopy
- **PK/PD:** hGH, lonapegsomatropin, mPEG, IGF-1, IGFBP-3

## Key Eligibility Criteria for Main Period Enrollment (All Regions)

- Adults and older adults with AGHD
- Ages 23 – 75 years
- GH treatment-naïve or no GH therapy in past 12 months
- IGF-1 SDS  $\leq$  -1.0 at screening

**Global:** Europe, North America, Asia (including Japan and China\*)

# TransCon hGH: New Paradigm for Growth Hormone Treatment

- In the phase 3 heiGHt Trial, TransCon hGH demonstrated superior AHV ( $P = 0.009$ ) with a comparable safety and tolerability profile compared to a daily hGH<sup>1</sup>
- In pediatric GHD, submitted BLA June 2020 and MAA September 2020 (including Auto-Injector):
  - FDA mid-cycle call held in December 2020, no advisory committee expected, PDUFA June 25, 2021
  - EMA MAA process and review underway, day 120 questions expected end of January
  - Received orphan designation in United States and Europe for GHD
  - PIP approved for children from 6 months to less than 18 years
- Global reach and label expansion:
  - China: Pediatric GHD phase 3 ongoing\*
  - Japan: Pediatric GHD phase 3 riGHt Trial, Clinical Trial Notification (CTN) filed Q3 2020
  - Adult GHD: Ongoing global phase 3 foresiGHt Trial, complete enrollment expected by late 2021 or early 2022
- Commercial manufacturing ongoing
- Multiple independent patent filings to provide potential IP protection into 2039

<sup>1</sup>Thornton P, et al. Oral presentation at ENDO 2019.  
\*Conducted by VISEN Pharmaceuticals.

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## TransCon PTH: PTH Replacement Therapy for Hypoparathyroidism

# Hypoparathyroidism

## Short-term Symptoms<sup>1</sup>

### 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<sup>2,3</sup>

**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<sup>4-6</sup>

**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*

<sup>1</sup> Nat Rev Dis Primers 2017 Aug 31;3:17055<sup>2</sup>Ascendis Pharma HP Patient Experience Research.  
<sup>3</sup>Endo Pract. 2014, 20(7);671-679. <sup>4</sup> J Bone Miner Res 2013, 28: 2570-2576; <sup>5</sup>J Clin Endocrinol Metab 2012, 97(12): 4507-4514. <sup>6</sup>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

- 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

# TransCon PTH Phase 2 Trial Design

**PaTHforward**  
TRIAL

59 adult subjects with HP currently receiving standard of care  
(active vitamin D + calcium); 1:1:1:1 randomization



## 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

PRO = Patient-reported Outcome. HPES = Hypoparathyroidism Patient Experience Scale.  
BMD = Bone Mineral Density. TBS = Trabecular Bone Score. DXA = Dual-Energy X-Ray  
Absorptiometry. FECa = Fractional Excretion of Calcium.

## Key Secondary Endpoints (4 weeks)

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

### Additional Endpoints ≥ 4 weeks

- PRO measures (including HPES and SF-36)
- Nephrolithiasis, nephrocalcinosis, vascular calcification, ER/urgent care visits and hospitalizations
- BMD and TBS by DXA, bone turnover markers, 24-hour urine calcium excretion (in extension only)

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- TransCon PTH was generally well-tolerated
- 58 out of 59 randomized subjects currently receiving 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 new safety signals identified in the OLE portion of the study

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

\*As of January 5, 2021.  
Preliminary PaTH Forward OLE 6-month data.  
TEAE = Treatment emergent adverse event

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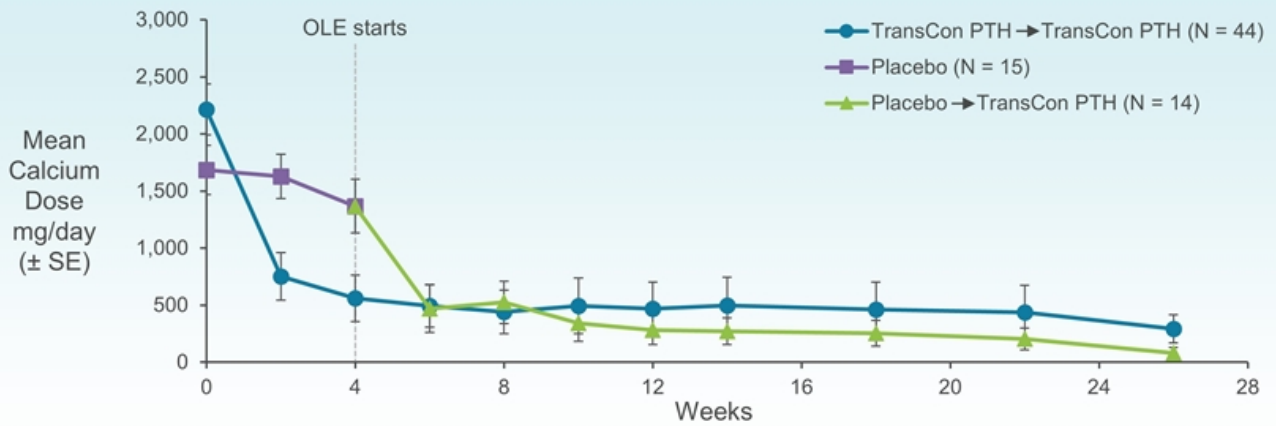
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# PaTH Forward OLE Mean Active Vitamin D Dose



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

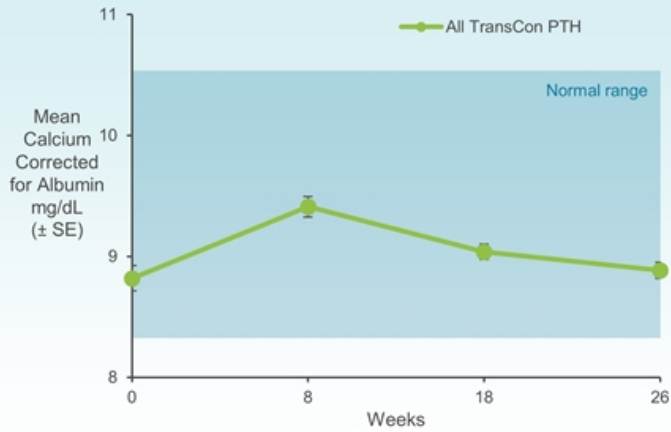
# PaTH Forward OLE Mean Calcium Supplement Dose



TransCon PTH enabled rapid and continuous calcium supplement reduction over 6-month study period

# PaTH Forward OLE 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



# PaTH Forward OLE Change in SF-36® Health Survey Domain Mean Scores (SD)

SF-36 Domain*	Placebo (N = 15)		Placebo Switch to TransCon PTH (N = 15)	TransCon PTH (N = 44)			All TransCon PTH (N = 59)	
	Baseline	Week 4	6 Months	Baseline	Week 4	6 Months	Baseline	6 Months
PF	45 (11)	46 (14)	51 (7)	46 (9)	51 (6)	52 (5)	46 (10)	51 (6)
RP	42 (10)	42 (14)	49 (11)	42 (10)	49 (8)	51 (6)	42 (10)	50 (7)
BP	43 (11)	40 (16)	46 (10)	46 (10)	49 (8)	51 (9)	45 (10)	50 (9)
GH	44 (10)	47 (11)	50 (7)	43 (10)	47 (8)	51 (9)	43 (10)	51 (8)
VT	44 (12)	43 (12)	52 (10)	42 (11)	49 (9)	53 (8)	43 (11)	53 (8)
SF	44 (11)	41 (15)	53 (5)	42 (10)	50 (8)	52 (6)	43 (10)	52 (6)
RE	45 (12)	39 (16)	51 (7)	42 (13)	49 (10)	50 (8)	43 (13)	50 (7)
MH	47 (9)	47 (11)	55 (5)	46 (9)	51 (8)	51 (8)	46 (9)	52 (7)
PCS	43 (12)	44 (14)	48 (8)	45 (10)	49 (7)	51 (7)	44 (11)	50 (8)
MCS	46 (10)	43 (12)	54 (6)	43 (11)	50 (9)	51 (8)	44 (11)	52 (8)

Preliminary PaTH Forward OLE 6-month data. Data on file.

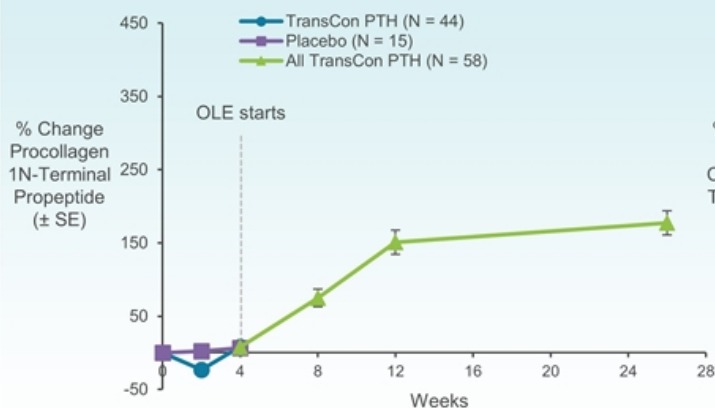
Green: Means above lower limit of population norm (47). (SD). \*PF (physical functioning), RP (role physical), BP (bodily pain), GH (general health), VT (vitality), SF (social functioning), RE (role emotional), MH (mental health), PCS (physical component summary), MCS (mental component summary).

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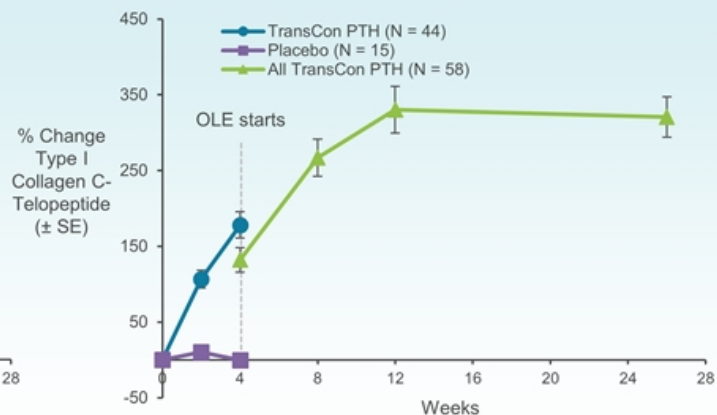


# PaTH Forward OLE % Change in Mean P1NP and CTx

### % Change in Mean P1NP



### % Change in Mean CTx



At 26-week point, observed lower level of increase for anabolic compared to catabolic bone turnover

# Bone Mineral Density by DXA

At baseline, mean BMD Z-scores\* at lumbar spine, femoral neck and total hip were elevated due to reduced bone turnover

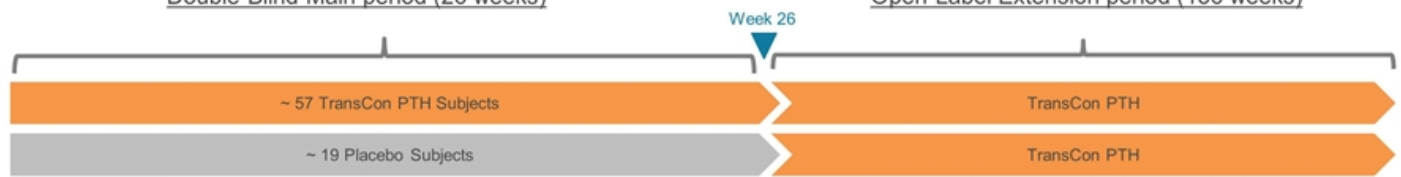
N = 44	Baseline	Week 26	Week 26 Change from Baseline
<b>Lumbar Spine L1-L4</b>			
Mean BMD Z-score	1.6	0.9	-0.7
<b>Femoral Neck</b>			
Mean BMD Z-score	1.2	0.7	-0.5
<b>Total Hip</b>			
Mean BMD Z-score	1.0	0.6	-0.5
<b>1/3 Radius</b>			
Mean BMD Z-score	0.4	0.4	0.0

With TransCon PTH treatment, BMD mean Z-score trended toward normalization at week 26

## Double-blind, placebo-controlled trial with an open-label extension period 76<sup>1</sup> adults with chronic hypoparathyroidism randomized 3:1 (TransCon PTH:placebo)

Double-Blind Main period (26 weeks)

Open-Label Extension period (156 weeks)



### 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  $\geq$  18 years
- Reliant on calcitriol  $\geq$  0.50 mcg per day or alfacalcidol  $\geq$  1.0 mcg per day, **and** therapeutic elemental calcium  $\geq$  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)

<sup>1</sup> Enrollment increased to 76 subjects to ensure evaluable data for 68.

<sup>2</sup> If needed to meet recommended dietary intake of calcium, it is permitted to take calcium supplements  $\leq$  600 mg/day as a nutritional supplement.

### 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<sup>2</sup>

### 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

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# TransCon PTH: A Potential PTH Replacement Therapy

- Phase 1 and phase 2\* data support profile of TransCon PTH as a potential PTH replacement therapy for HP
- Preliminary phase 2 PaTH Forward OLE results at month 6\*:
  - 86% of subjects had (1) normal serum calcium, (2) off active vitamin D and (3) taking  $\leq$  600 mg/day of calcium
  - Mean scores for all summary and subdomains of SF-36 were normal for all TransCon PTH subjects at 6 months in PaTH Forward OLE
  - 58 out of 59 randomized subjects currently receiving TransCon PTH in OLE\*\*
  - 12-month OLE update anticipated in Q2 2021
- Received orphan designation in US and EU
- Expect to file CTN for Japanese adult HP phase 3 study in Q2 2021
- North American and European phase 3 PaTHway Trial results expected Q4 2021

\*Preliminary PaTH Forward OLE 6-month data. Data on file.  
\*\*As of January 5, 2021.

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# TransCon CNP: The New Frontier of Growth Biology

# 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



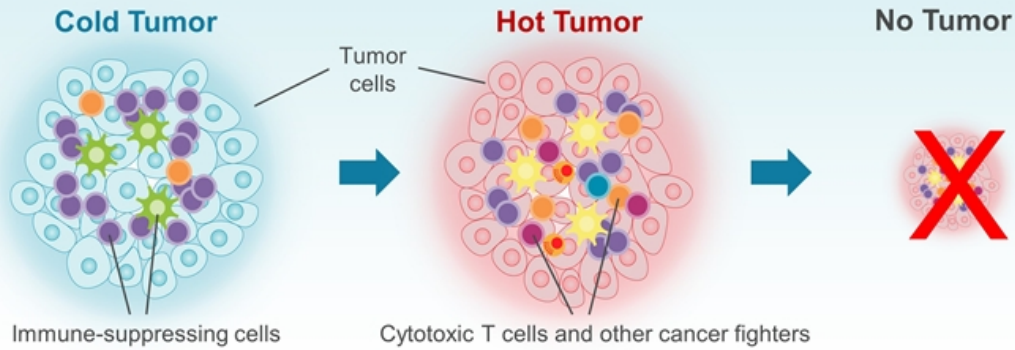
# Oncology



# TransCon Positioned to Transform Cancer Therapy

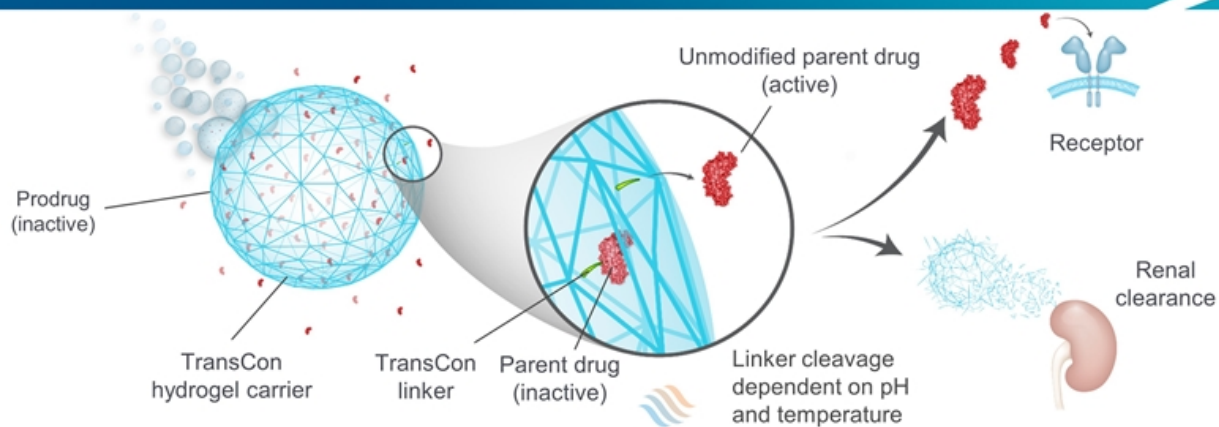
TransCon systemic and intratumoral technologies designed to enhance anti-tumor effects by

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



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

# TransCon Technology: Sustained Localized Release



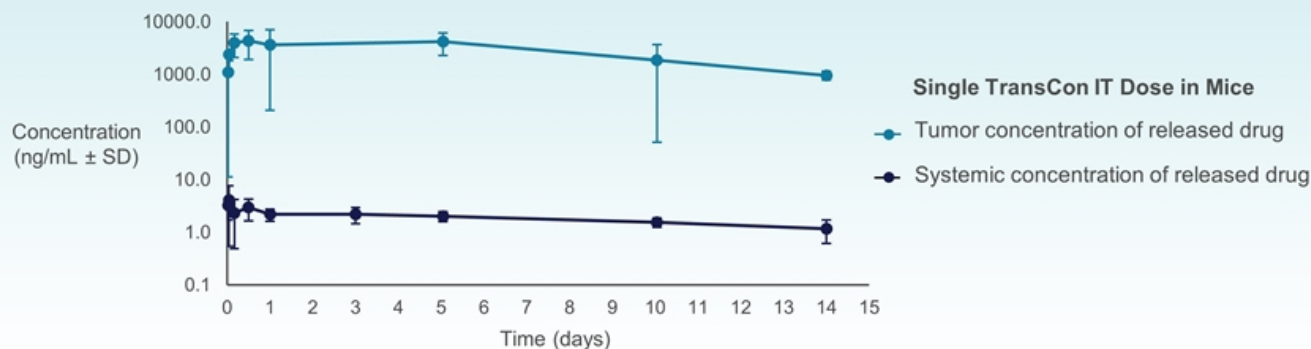
Parent drug is transiently bound to TransCon linker-hydrogel carrier, which inactivates, shields parent drug and prevents clearance

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

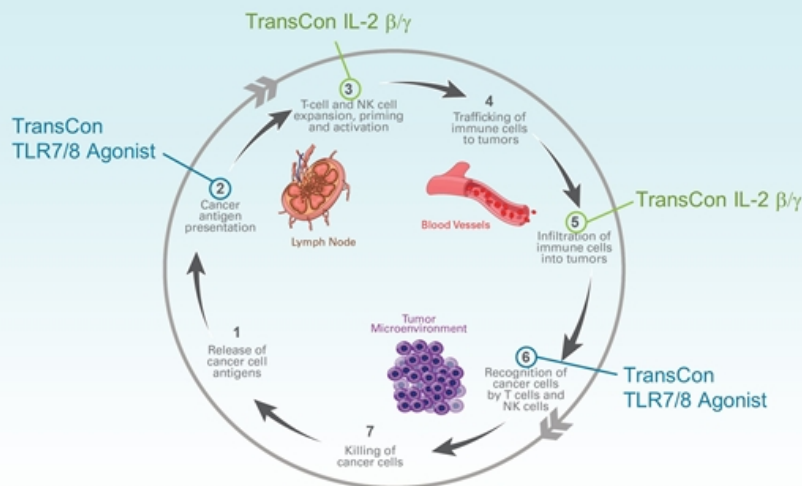
# TransCon IT: Potential Paradigm Shift in Intratumoral Delivery

TransCon Intratumoral (IT) addresses the problems of conventional IT administration 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

# Two Near-term Clinical Candidates – Potential to Address All 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 filed)

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

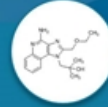
Designed to aid T cell and NK cell expansion and infiltration of immune cells into tumors (IND or similar planned for Q3 2021)

### Additional TransCon Candidates

One IND or similar filing each year for 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 TLR7/8 Agonist



TransCon TLR7/8  
Agonist

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

## 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

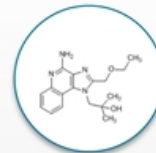
## Safety

- 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 IT, sustained release with **minimal systemic exposure** aiming for **superior efficacy**

# Phase 1/2 Dose Escalation and Dose Expansion Study of TransCon TLR7/8 Agonist Alone or in Combination with CPI

Dose Escalation ("3 + 3" Design)

Dose Expansion

**Part 1:  
Monotherapy**

Any solid tumor,  
any line

**Part 2:  
Combination with CPI**

Indications with known  
CPI activity

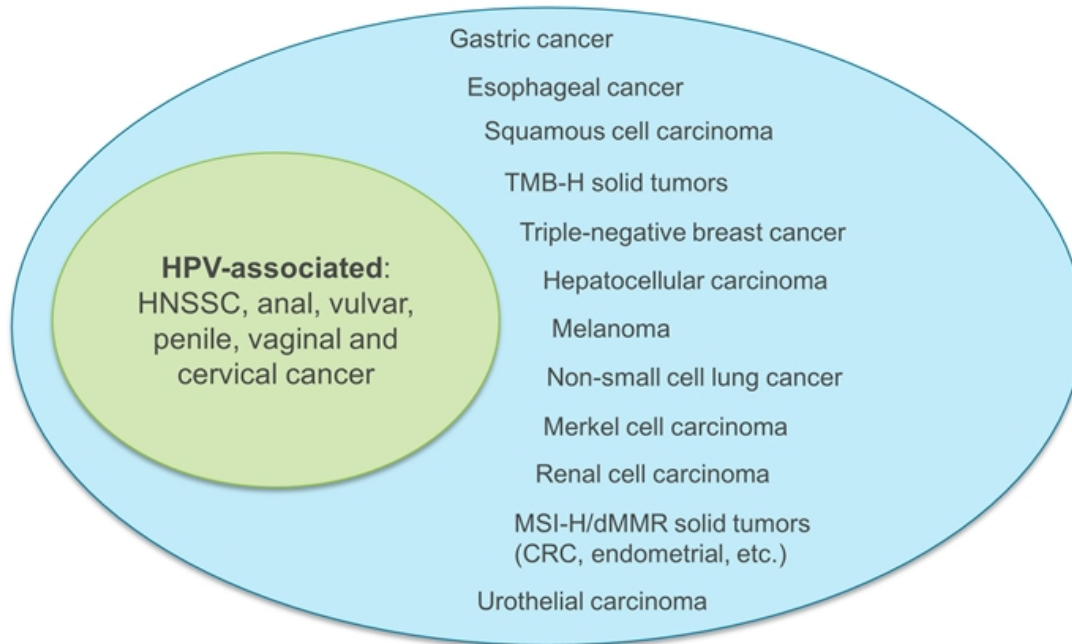
**Part 3:  
Combination with CPI**

Multiple indication-specific  
cohorts at Recommended  
Ph2 Dose (RP2D)

**Objectives:**

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

## Initial Indication Selection Based on Strong Scientific Rationale to Focus on HPV-associated Cancers





## 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 expected to enable superior efficacy
- IND filed December 2020
- Focus on HPV-associated tumors as first indications
- Initiation of CPI combo dose escalation expected Q2 2021
- Initial results for monotherapy dose escalation expected Q4 2021

# TransCon IL-2 $\beta/\gamma$



TransCon  
IL-2  $\beta/\gamma$

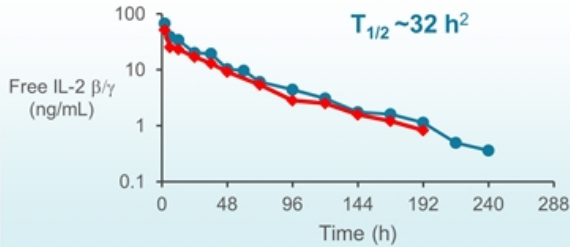
All product candidates are investigational. For investor communication only. Not for use in promotion or product commercialisation.

# TransCon IL-2 $\beta/\gamma$ : Optimized $\beta/\gamma$ Bias, Potency and PK

Variant	$\beta/\gamma$ Bias	Potency Reduction <sup>1</sup>
IL-2	No	n/a
IL-2 $\beta/\gamma$ 5 kDa	Yes	~4-fold
IL-2 $\beta/\gamma$ 10 kDa	Yes	~6-fold
IL-2 $\beta/\gamma$ 30 kDa	Yes	~20-fold



Optimizing IL-2  $\beta/\gamma$  bias and potency through permanent PEGylation



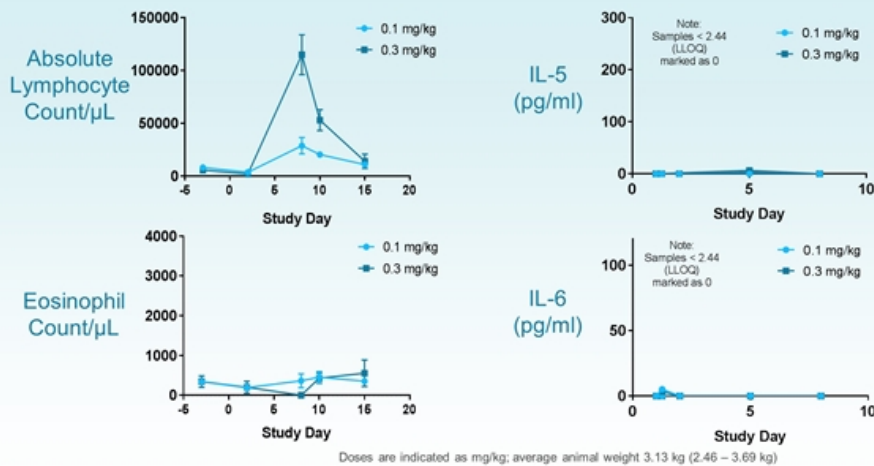
TransCon technology provides low  $C_{\text{max}}$  and prolonged exposure

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

40 \*Data on file. <sup>1</sup>Potency determined in HH cell-based assay expressing IL-2R  $\beta/\gamma$ .  
<sup>2</sup>NHP Study Dose: 0.1 mg/kg.

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

## TransCon IL-2 $\beta/\gamma^1$ (Single Dose on Day 1)



- 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<sup>3,4</sup>

Q3W = every 3 weeks.

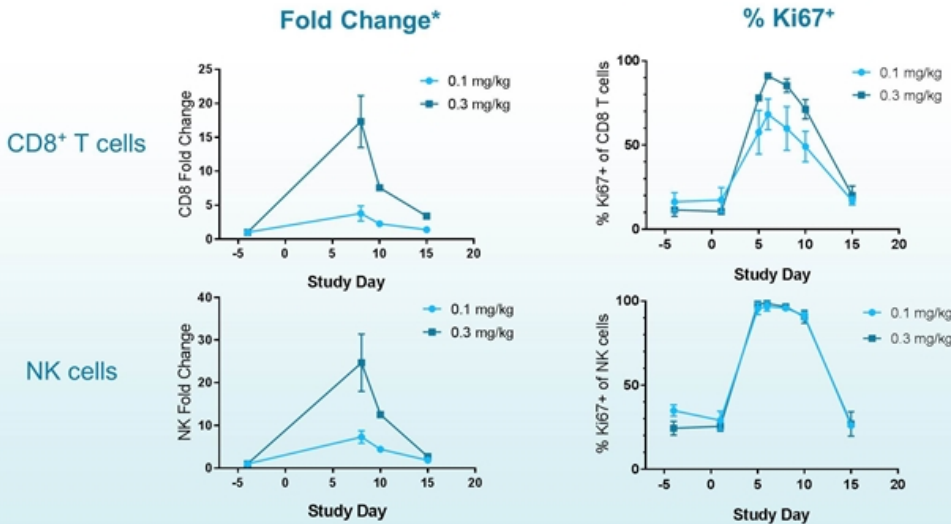
<sup>1</sup>Data on file. <sup>2</sup>Rosen D, et al. AACR annual meeting. 2020; Poster 4507.

41 | <sup>3</sup>Rand, et al. *J Clin Invest.* 1991; 88: 825. <sup>4</sup>Van Haelst Pisanic C, et al. *Blood.* 1991;78:1538.

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ascendis  
pharma

# Potent CD8<sup>+</sup> T Cell and NK Cell Peripheral Expansion and Activation in NHP



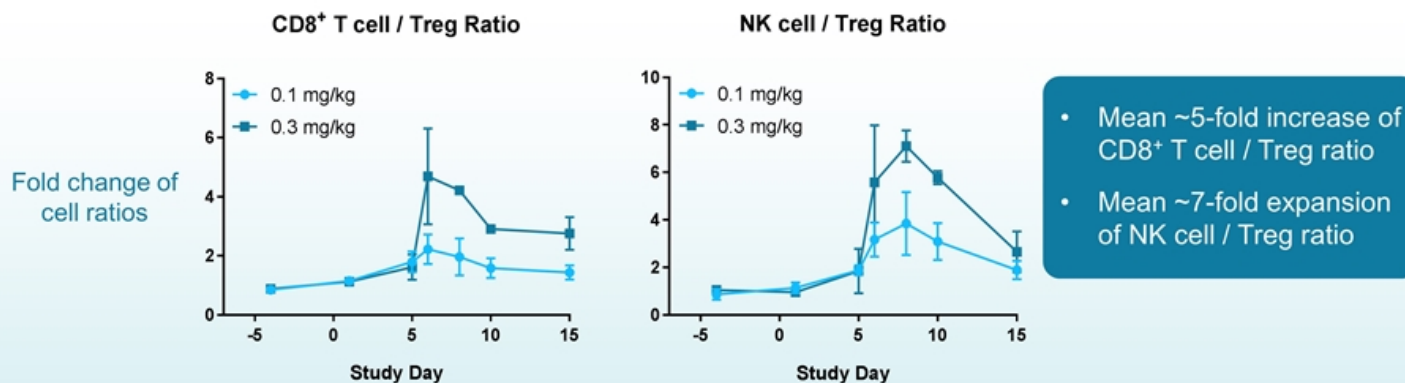
- Mean ~17-fold expansion of CD8<sup>+</sup> T cells
- Mean ~25-fold expansion of NK cells
- Almost 100% of cells expressing Ki67 activation marker

Expansion and activation of cytotoxic lymphocyte subsets observed following a single dose of TransCon IL-2  $\beta/\gamma$

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

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

# TransCon IL-2 $\beta/\gamma$ Expands Ratios of CD8<sup>+</sup> T Cells and NK Cells Over Treg Cells in NHP



A single dose of TransCon IL-2  $\beta/\gamma$  resulted in durable and robust increases in the ratios of CD8<sup>+</sup> T cells and NK cells over Treg cells in NHP

# Evaluation of Immune Memory and Potential Cross-immunity Following TransCon IL-2 $\beta/\gamma$ plus TransCon TLR7/8 Agonist

Syngeneic CT26 tumor model  
(colon-derived tumor line)

Treatment with TransCon IL-2  $\beta/\gamma$   
+ TransCon TLR7/8 Agonist

Re-challenge of complete  
responders with CT26

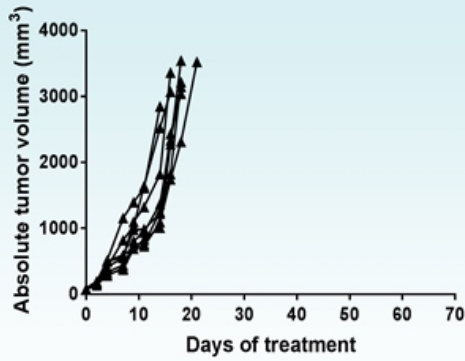
- 73 days after initial treatment
- No additional treatment

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

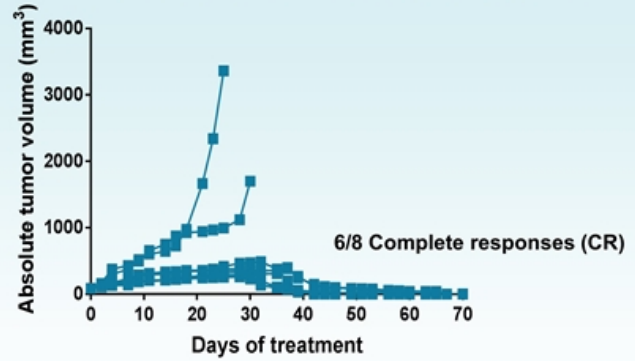
- 28 days after CT26 re-challenge
- No additional treatment

# TransCon IL-2 $\beta/\gamma$ Plus TransCon TLR7/8 Agonist Resulted in Durable Complete Tumor Regressions in the CT26 Tumor Model

Buffer control



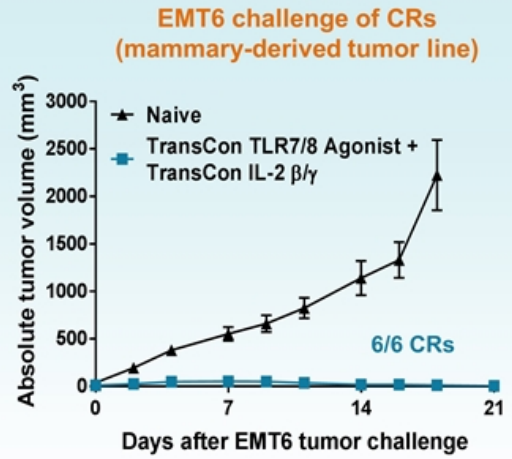
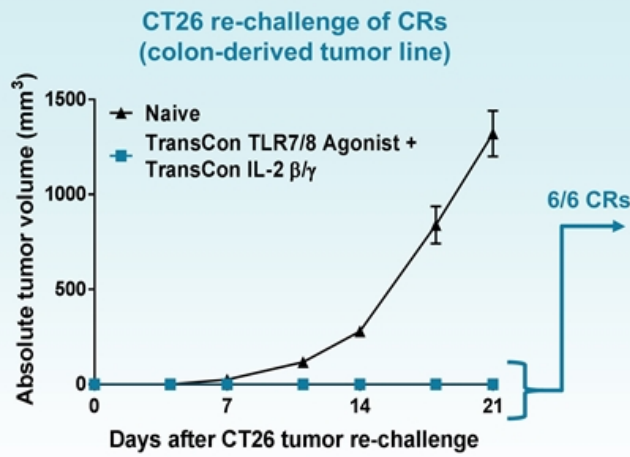
TransCon IL-2  $\beta/\gamma$  (3 doses) +  
TransCon TLR7/8 Agonist (single dose)



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



# 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

## 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 superior efficacy with minimal systemic adverse events; IND filed
  - TransCon IL-2  $\beta/\gamma$  designed for optimized IL-2R $\beta/\gamma$  bias and potency, combined with low  $C_{max}$  and long exposure; IND or similar planned for Q3 2021
  - Combination resulted in potent anti-tumor responses and immunological memory, including cross-immunity against a new tumor type
- Building diversified pipeline through one IND or similar filing each year for new TransCon product candidates with the potential to affect all steps in the immunity cycle

## 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 potential launch of TransCon hGH in pediatric GHD
- Preparing for 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 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
  - In Series A financing, Vivo and Sofinnova invested \$40 million, and Ascendis contributed rights to TransCon hGH, TransCon PTH and TransCon CNP for 50% equity ownership
- 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
  - Ascendis now owns ~44% of issued and outstanding shares
- Following closing of the Series B financing, Ascendis has an additional board seat:
  - Michael Wolff Jensen, Chairman, Senior Vice President and Chief Legal Officer of Ascendis, became a member of VISEN's board and serves as Chairman
  - Jan Mikkelsen, CEO of Ascendis will continue to serve on the VISEN board

# Selected 2021 Expected Key Milestones





**Ascendis Pharma A/S Provides Vision 3x3 Update at  
39th Annual J.P. Morgan Healthcare Conference**

**COPENHAGEN, Denmark, January 10, 2021/ Globe Newswire/** – Ascendis Pharma A/S (Nasdaq: ASND), a biopharmaceutical company that utilizes its innovative TransCon™ technologies to create product candidates that address unmet medical needs, will provide an update on Vision 3x3 and the company's 2021 key milestones at the 39th Annual J.P. Morgan Healthcare Conference.

“In 2019, we introduced Vision 3x3, the company's strategic roadmap through 2025, to build a leading biopharma company by achieving sustainable growth through multiple approaches. 2020 was a remarkable year of progress for Ascendis reflecting the dedication and commitment of our employees worldwide as we made meaningful strides to achieve our vision, and meet or accelerate completion of our key milestones,” said Jan Mikkelsen, Ascendis Pharma's President and Chief Executive Officer.

“We expect 2021 will mark a number of key clinical and commercial milestones. By the end of the year, we expect to have five independent TransCon product candidates in clinical development leveraging TransCon technologies through our algorithm for product innovation. We expect to further advance our late stage endocrinology pipeline with the anticipated approval and launch in the United States and the approval in Europe of TransCon hGH for pediatric growth hormone deficiency, and to obtain phase 3 results for TransCon PTH in adult hypoparathyroidism. Development of TransCon CNP is progressing as planned with the recent initiation by VISEN Pharmaceuticals of a second phase 2 trial in patients with achondroplasia, the ACcomplish China Trial, which provides for dose expansion at an effective dose determined from the ACcomplish Trial. Finally, we expect to have the first two product candidates from our second therapeutic area of oncology in clinical development,” Mr. Mikkelsen added.

**Pipeline Updates**

- **TransCon hGH (lonapegsomatropin):** Lonapegsomatropin is an investigational long-acting prodrug of somatropin (human growth hormone or hGH) currently under review for use in pediatric growth hormone deficiency (GHD) by the United States Food and Drug Administration (FDA) and the European Medicines Agency (EMA):
  - The company submitted its Biologic License Application to the FDA which has set a Prescription Drug User Fee Act (PDUFA) date for June 25, 2021. If approved on the PDUFA date, Ascendis anticipates commercial launch in the third quarter of 2021.
  - The company submitted its Marketing Authorisation Application (MAA) to the EMA in September 2020 and anticipates receiving MAA approval for lonapegsomatropin for use in pediatric GHD in the fourth quarter of 2021.
  - Ascendis anticipates completion of enrollment in foresiGHt, a global phase 3 trial evaluating the safety and efficacy of lonapegsomatropin in adult patients with GHD, by late 2021 or early 2022.

- **TransCon PTH:** TransCon PTH is an investigational long-acting prodrug of parathyroid hormone (PTH) in development as a potential once-daily replacement therapy for adult hypoparathyroidism (HP):
  - From the PaTH Forward phase 2 trial, 58 out of 59 randomized subjects continue receiving TransCon PTH in the open label extension (OLE) as of January 5, 2021.
  - After 26 weeks of follow-up in the PaTH Forward Trial, bone densitometry data from subjects treated with TransCon PTH demonstrated trends towards normalization of bone mineral density. In addition, quality of life as measured by the SF-36® Health Survey showed normalization of mean scores for all summary domains and all subdomains.
  - During the second quarter of 2021, Ascendis expects to provide a 12-month OLE update and plans to submit a Clinical Trial Notification for a clinical trial evaluating TransCon PTH for adult HP in Japan.
  - Top-line results from PaTHway, a phase 3 randomized, double-blind, placebo-controlled clinical trial in North America and Europe, investigating the safety, tolerability, and efficacy of TransCon PTH in adults with HP are expected in the fourth quarter of 2021.
- **TransCon CNP:** TransCon CNP, an investigational long-acting prodrug of C-type natriuretic peptide (CNP), as a potential therapeutic option for patients with achondroplasia (ACH):
  - Dosing of sequential ascending dose cohorts continues in the ACcomplisH Trial, a phase 2 randomized, double-blind, placebo-controlled clinical trial in North America, Europe, and Oceania.
  - VISEN Pharmaceuticals (VISEN), our strategic investment in China, received approval from China's Center for Drug Evaluation to conduct the ACcomplisH China Trial, a phase 2 randomized, double-blind, placebo-controlled clinical trial.
  - Ascendis expects that the ACcomplisH and ACcomplisH China Trials will enroll more than 120 subjects in total (ages 2-10), to be followed for 12 months.
  - The company plans to provide a TransCon CNP clinical program update in the fourth quarter of 2021.
- **TransCon TLR7/8 Agonist:** TransCon TLR7/8 Agonist is an investigational long-acting prodrug of resiquimod, a small molecule agonist of Toll-like receptors (TLR) 7 and 8 designed to provide sustained activation of intratumoral antigen-presenting cells driving tumor antigen presentation and induction of immune stimulatory cytokines for weeks or months with a single intratumoral injection:
  - Submitted IND to the FDA in December 2020 to initiate clinical program.
  - During the second quarter of 2021, following monotherapy evaluation, the company plans to initiate TransCon TLR7/8 Agonist dose escalation in combination with a checkpoint inhibitor.
  - Initial monotherapy dose escalation results are expected in the fourth quarter of 2021.
- **TransCon IL-2 β/g:** TransCon IL-2 β/g is an investigational novel long-acting prodrug of IL-2 β/g designed to selectively bind and activate the IL-2Rβ/g:
  - Ascendis reported pre-clinical data for TransCon IL-2 β/g demonstrating:
    - Independently optimized receptor bias and potency as well as pharmacokinetics to create a potentially best-in-class IL-2 product.
    - An effective half-life of approximately 32 hours in non-human primates (NHP).

- Following a single dose of TransCon IL-2 b/g in NHP, observed potential best-in-class expansion and activation of cytotoxic lymphocyte subsets with minimal effect on eosinophils, minimal IL-5 and IL-6 levels which suggests low risk of vascular leak syndrome.
- The company expects to submit an IND or similar for TransCon IL-2 b/g in the third quarter of 2021.

#### **Global Endocrinology Rare Disease Commercial Strategy**

In anticipation of regulatory approvals for lonapegsomatropin in the United States and Europe, Ascendis is establishing a global commercial presence through multiple approaches. This global commercial approach will be laying the groundwork for future potential endocrinology rare disease launches as TransCon PTH and TransCon CNP advance in clinical development.

The company's US commercial organization is in place and commercial manufacturing is ongoing for the potential launch of lonapegsomatropin in pediatric GHD planned for the third quarter of 2021 after anticipated regulatory approval.

In addition, Ascendis is preparing for potential commercialization in Europe, building an integrated organization in select European countries and evaluating established distribution channels in other European countries to be ready for the anticipated MAA approval of lonapegsomatropin in pediatric GHD in the fourth quarter of 2021.

Lastly, Ascendis plans to serve patients in other regions around the world through established sales and distribution networks and following applicable regulatory approvals. The company has invested in VISEN in Greater China and plans to partner in Japan and South Korea when appropriate.

#### **Presentation at J.P. Morgan Healthcare Conference on Monday, January 11<sup>th</sup>**

Live webcast of the J.P. Morgan presentation will be available on the Events & Presentations section of the investor relations webpage at <https://investors.ascendispharma.com/events-and-presentations>. The presentation will begin at 11:40 a.m. ET. A webcast replay will also be available for 30 days.

The company's slides from the J.P. Morgan presentation will be available on the investor relations website.

#### **About TransCon™ Technology Platform**

TransCon refers to "transient conjugation." The proprietary TransCon platform is an innovative technology to create new therapies that are designed to optimize therapeutic effect, including efficacy and safety and through dosing frequency. TransCon molecules have three components: an unmodified parent drug, an inert carrier that protects it, and a linker that temporarily binds the two. When bound, the carrier inactivates and shields the parent drug from clearance. When injected into the body, physiologic conditions (e.g., pH and temperature) initiate the release of the active, unmodified parent drug in a predictable manner. Because the parent drug is unmodified, its original mode of action is expected to be maintained. The TransCon technology platform can be applied broadly to proteins, peptides or small molecules in multiple therapeutic areas, and can be designed for systemic or localized release.

#### **About Ascendis Pharma A/S**

Ascendis Pharma is applying its innovative TransCon technologies to build a leading, fully integrated biopharmaceutical company focused on making a meaningful difference in patients' lives. Guided by its core values of patients, science and passion, the company utilizes its TransCon technologies to create new and potentially best-in-class therapies.



Ascendis Pharma currently has a pipeline of three independent endocrinology rare disease product candidates in clinical development and is advancing oncology as its second therapeutic area of focus. The company continues to expand into additional therapeutic areas to address unmet patient needs.

Ascendis is headquartered in Copenhagen, Denmark, with additional offices in Heidelberg and Berlin, Germany, Palo Alto and Redwood City, California, and Princeton, New Jersey.

For more information, please visit [www.ascendispharma.com](http://www.ascendispharma.com).

### **Forward-Looking Statements**

This press release contains forward-looking statements that involve substantial risks and uncertainties. All statements, other than statements of historical facts, included in this press release regarding Ascendis' future operations, plans and objectives of management are forward-looking statements. Examples of such statements include, but are not limited to, statements relating to (i) Ascendis' expectation that 2021 will mark a number of key milestones (ii) Ascendis' expectation that by the end of 2021 it will have five independent TransCon product candidates in clinical development, (iii) Ascendis' expectations regarding the timing of potential approval and launch of TransCon hGH (lonapegsomatropin), (iv) Ascendis' expectations regarding when it will obtain phase 3 results for TransCon PTH in adult hypoparathyroidism, (v) Ascendis' expectation that it will have the first two product candidates from its second therapeutic area of oncology in clinical development in 2021, (vi) Ascendis' ability to apply its platform technology to build a leading, fully integrated biopharmaceutical company, (vii) Ascendis' product pipeline and expansion into additional therapeutic areas and (viii) Ascendis' expectations regarding its ability to utilize its TransCon technologies to create new and potentially best-in-class therapies. Ascendis may not actually achieve the plans, carry out the intentions or meet the expectations or projections disclosed in the forward-looking statements and you should not place undue reliance on these forward-looking statements. Actual results or events could differ materially from the plans, intentions, expectations and projections disclosed in the forward-looking statements. Various important factors could cause actual results or events to differ materially from the forward-looking statements that Ascendis makes, including the following: unforeseen safety or efficacy results in its oncology programs, TransCon hGH, TransCon PTH and TransCon CNP or other development programs; unforeseen expenses related to the development and potential commercialization of its oncology programs, TransCon hGH, TransCon PTH and TransCon CNP or other development programs; selling, general and administrative expenses, other research and development expenses and Ascendis' business generally; delays in the development of its oncology programs, TransCon hGH, TransCon PTH and TransCon CNP or other development programs related to manufacturing, regulatory requirements, speed of patient recruitment or other unforeseen delays; dependence on third party manufacturers to supply study drug for planned clinical studies; Ascendis' ability to obtain additional funding, if needed, to support its business activities and the effects on its business of the worldwide COVID-19 pandemic. For a further description of the risks and uncertainties that could cause actual results to differ from those expressed in these forward-looking statements, as well as risks relating to Ascendis' business in general, see Ascendis' prospectus supplement filed on July 9, 2020 and Ascendis' current and future reports filed with, or submitted to, the U.S. Securities and Exchange Commission (SEC), including its Annual Report on Form 20-F filed with the SEC on April 3, 2020. Forward-looking statements do not reflect the potential impact of any future in-

licensing, collaborations, acquisitions, mergers, dispositions, joint ventures, or investments that Ascendis may enter into or make. Ascendis does not assume any obligation to update any forward-looking statements, except as required by law.

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