TransCon™ CNP
ACcomplisH Trial Topline Results

November 14, 2022

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Executive Summary

- In the Phase 2 ACcomplisH Trial in children with achondroplasia aged 2-10, once-weekly TransCon CNP demonstrated the potential to meet patient and caregiver needs for a safe, effective, tolerable, and convenient treatment
- The primary endpoint, annualized height velocity (AHV) at Week 52, demonstrated superiority of TransCon CNP at 100 µg/kg/week compared to placebo (p=0.0218)
- TransCon CNP was generally well tolerated with low frequency of injection site reactions; all 57 randomized children continued, with the longest treatment duration beyond two years
- Data showed robust and consistent results in prespecified analyses across age groups and dose levels, supporting continued development at the selected dose of 100 µg/kg/week

ANCOVA model. Data on file, Ascendis Pharma 2022.

TransCon CNP: Phase 2 Trial Design

ACcomplisH TRIAL

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

TransCon CNP vs. placebo (3:1 randomization)

12 subjects randomized in each dose cohort in a blinded manner

6 µg/kg → **20** µg/kg → **50** µg/kg → **100** µg/kg → **>100** µg/kg

Data Monitoring Committee reviews blinded data after each dose cohort

Open Label Extension Period to evaluate long-term safety and efficacy

Primary Endpoint

- Annualized height velocity

Key Secondary/Additional Endpoints

- Change in body proportionality
- Patient reported outcome (PRO) measures
- Exploratory biomarkers evaluated

ClinicalTrials.gov. https://clinicaltrials.gov/ct2/show/NCT04085523?term=ACcomplisH&draw=2&rank=5. Accessed 05/23/2021.

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Demographics and Baseline Characteristics

	TransCon CNP 6 µg/kg/week n=10	TransCon CNP 20 µg/kg/week n=11	TransCon CNP 50 µg/kg/week n=10	TransCon CNP 100 µg/kg/week n=11	Total TransCon CNP n=42	Total Placebo n=15
Age (years)						
Mean (SD)	6.5 (2.6)	6.3 (2.9)	5.2 (3.0)	5.8 (2.6)	6.0 (2.7)	5.9 (3.1)
Median (Min, Max)	6.8 (2.3, 10.7)	7.3 (2.7, 11.0)	4.7 (2.1, 10.1)	5.4 (2.1, 9.9)	5.6 (2.1, 11.0)	4.9 (2.4, 11.0)
Age Group (years) – n (%)						
< 5 years	3 (30.0)	5 (45.5)	5 (50.0)	3 (27.3)	16 (38.1)	8 (53.3)
≥ 5 years	7 (70.0)	6 (54.5)	5 (50.0)	8 (72.7)	26 (61.9)	7 (46.7)
Sex – n (%)						
Female	7 (70.0)	3 (27.3)	3 (30.0)	6 (54.5)	19 (45.2)	5 (33.3)
Male	3 (30.0)	8 (72.7)	7 (70.0)	5 (45.5)	23 (54.8)	10 (66.7)
Race – n (%)						
White	8 (80.0)	10 (90.9)	8 (80.0)	10 (90.9)	36 (85.7)	12 (80.0)
Other	2 (20.0)	1 (9.1)	2 (20.0)	1 (9.1)	6 (14.3)	3 (20.0)

Data on file, Ascendis Pharma 2022.

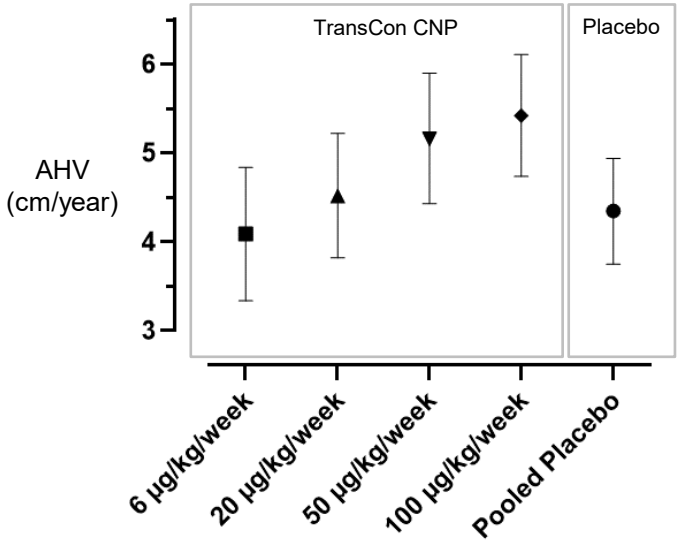
Demographics and Baseline Characteristics (continued)

	TransCon CNP 6 µg/kg/week n=10	TransCon CNP 20 µg/kg/week n=11	TransCon CNP 50 µg/kg/week n=10	TransCon CNP 100 µg/kg/week n=11	Total TransCon CNP n=42	Total Placebo n=15
Height (cm)						
Mean (SD)	90.63 (8.97)	92.29 (12.10)	86.61 (12.97)	89.23 (12.82)	89.74 (11.61)	90.85 (14.92)
Median (Min, Max)	90.25 (73.70, 101.77)	93.70 (78.20, 111.17)	84.70 (72.10, 105.87)	90.23 (69.40, 111.53)	90.08 (69.40, 111.53)	89.70 (70.47, 113.37)
Height SDS*						
Mean (SD)	-5.45 (1.05)	-4.87 (0.67)	-4.85 (0.80)	-4.92 (0.83)	-5.02 (0.85)	-4.85 (0.96)
Median (Min, Max)	-5.80 (-6.56, -3.92)	-4.66 (-6.15, -4.10)	-5.14 (-6.03, -3.66)	-4.64 (-6.16, -3.74)	-5.12 (-6.56, -3.66)	-4.69 (-6.73, -3.32)
Height SDS, ACH-Specific**						
Mean (SD)	-0.20 (0.70)	0.28 (0.68)	0.21 (0.67)	0.11 (0.77)	0.11 (0.70)	0.43 (0.91)
Median (Min, Max)	-0.36 (-1.31, 0.66)	0.28 (-0.89, 1.21)	0.09 (-0.55, 1.46)	0.02 (-1.16, 1.33)	0.02 (-1.31, 1.46)	0.65 (-1.18, 2.08)

* CDC 2000 Stature-for-Age Charts, https://www.cdc.gov/growthcharts/data_tables.htm, accessed 13 Nov 2022.
** Hoover-Fong JE, Schulze KJ, Alade AY, et al. Growth in achondroplasia including stature, weight, weight-for-height and head circumference from CLARITY. *Orphanet J Rare Dis*. 2021;16(1):522.

TransCon CNP 100 µg/kg/week Demonstrated Superiority in AHV Compared to Placebo

Treatment Group (TransCon CNP Dose Levels or Placebo)	AHV (cm/year), n LS Mean [95% CI]	p-value (TransCon CNP vs. Pooled Placebo)
6 µg/kg/week	4.09, n=10 [3.34, 4.84]	0.6004
20 µg/kg/week	4.52, n=11 [3.82, 5.22]	0.7022
50 µg/kg/week	5.16, n=10 [4.43, 5.90]	0.0849
100 µg/kg/week	5.42, n=11 [4.74, 6.11]	0.0218
Pooled Placebo	4.35, n=15 [3.75, 4.94]	NA



TransCon CNP demonstrated a dose-response in AHV across the four dose groups

ANCOVA model.

Data on file, Ascendis Pharma 2022.

Comparable AHV Across Age Groups

Treatment Group (TransCon CNP Dose Levels or Placebo)	Age <5 years old	Age ≥5 years old
	AHV (cm/year), n LS Mean, [95% CI]	AHV (cm/year), n LS Mean, [95% CI]
6 µg/kg/week	4.31, n=3 [2.52, 6.10]	3.79, n=7 [2.87, 4.71]
20 µg/kg/week	4.72, n=5 [3.30, 6.15]	4.29, n=6 [3.43, 5.15]
50 µg/kg/week	5.07, n=5 [3.62, 6.52]	5.33, n=5 [4.39, 6.26]
100 µg/kg/week	5.95, n=3 [4.03, 7.87]	5.12, n=8 [4.35, 5.90]
Pooled Placebo	4.53, n=8 [3.43, 5.63]	4.29, n=7 [3.44, 5.14]

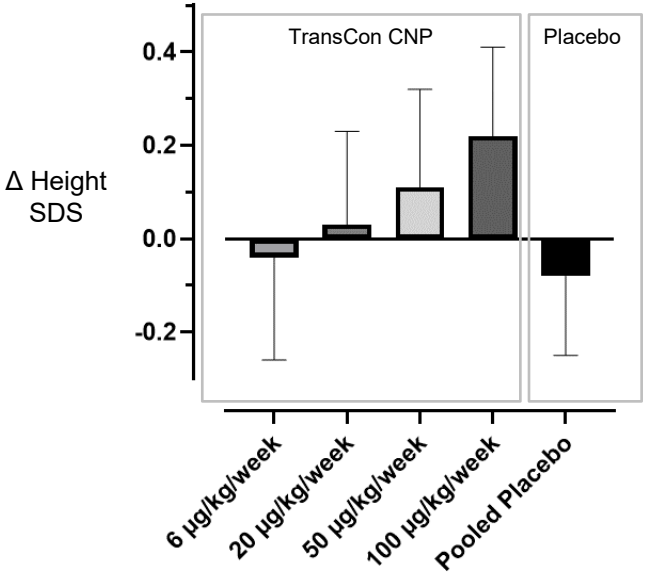
Consistent dose-dependent treatment effect across age groups

ANCOVA model.

Data on file, Ascendis Pharma 2022.

TransCon CNP 100 µg/kg/week Demonstrated Superiority in Change in ACH-Specific Height SDS Compared to Placebo

Treatment Group (TransCon CNP Dose Levels or Placebo)	Δ Height SDS*, n LS Mean [95% CI]	p-value (TransCon CNP vs. Pooled Placebo)
6 µg/kg/week	-0.04, n=10 [-0.26, 0.17]	0.8207
20 µg/kg/week	0.03, n=11 [-0.17, 0.23]	0.4107
50 µg/kg/week	0.11, n=10 [-0.10, 0.32]	0.1660
100 µg/kg/week	0.22, n=11 [0.02, 0.41]	0.0283
Pooled Placebo	-0.08, n=15 [-0.25, 0.10]	NA



TransCon CNP demonstrated a dose-dependent improvement in ACH-specific height SDS across all dose groups

* Hoover-Fong JE, Schulze KJ, Alade AY, et al. Growth in achondroplasia including stature, weight, weight-for-height and head circumference from CLARITY. *Orphanet J Rare Dis*. 2021;16(1):522. ANCOVA model

Safety Results Summary (Double-Blind Period)

- TransCon CNP was generally well tolerated, with no discontinuations
  - Frequency of TEAEs in each dose group was similar to placebo
- No serious AEs (SAEs) related to treatment were reported
  - Two unrelated SAEs were reported (febrile convulsion and viral infection)
- 95% of TransCon CNP patients and 93% of placebo patients reported TEAEs
  - 95% of TransCon CNP TEAEs were assessed as mild (Grade 1) in severity
- Injections were generally well tolerated with low frequency of injection site reactions
- No reported events of symptomatic hypotension
- For body proportionality, induced growth was proportional across all groups at Week 52

Observed safety results support continued development of TransCon CNP for children with achondroplasia

TEAE : Treatment emergent adverse event

Data on file, Ascendis Pharma 2022.

Overview of TEAEs (Double-Blind Period)

	TransCon CNP 6 µg/kg/week (n=10)	TransCon CNP 20 µg/kg/week (n=11)	TransCon CNP 50 µg/kg/week (n=10)	TransCon CNP 100 µg/kg/week (n=11)	Total Placebo (n=15)
Subjects with TEAEs*	9 (90.0)	11 (100.0)	10 (100.0)	10 (90.9)	14 (93.3)
Grade 1 (mild)	9 (90.0)	11 (100.0)	10 (100.0)	9 (81.8)	14 (93.3)
Grade 2 (moderate)	3 (30.0)	3 (27.3)	3 (30.0)	1 (9.1)	5 (33.3)
Serious TEAEs	1 (10.0)	0	1 (10.0)	0	0
Treatment-Related TEAEs	3 (30.0)	2 (18.2)	3 (30.0)	2 (18.2)	5 (33.3)
Achondroplasia-Related TEAEs**	3 (30.0)	4 (36.4)	5 (50.0)	1 (9.1)	9 (60.0)

* No reported Grade 3 (severe) or Grade 4 (life-threatening) TEAEs.
**Adverse events reported by investigator as related to underlying disease.

Data on file, Ascendis Pharma 2022.

Treatment-Related Adverse Events (Double-Blind Period)

	TransCon CNP 6 µg/kg/week (n=10)	TransCon CNP 20 µg/kg/week (n=11)	TransCon CNP 50 µg/kg/week (n=10)	TransCon CNP 100 µg/kg/week (n=11)	Total Placebo (n=15)
Subjects with at Least One Treatment-Related TEAE	3 (30.0)	2 (18.2)	3 (30.0)	2 (18.2)	5 (33.3)
Injection site reactions (ISRs)*	2 (20.0)	1 (9.1)	3 (30.0)	2 (18.2)	2 (13.3)
Abdominal pain upper	0	1 (9.1)	0	0	0
Overdose	0	0	0	0	1 (6.7)
Dizziness	0	0	0	0	1 (6.7)
Sleep terror	0	0	0	0	1 (6.7)
Urticaria	1 (10.0)	0	0	0	0

Injections were generally well tolerated with low frequency of injection site reactions
11 mild ISRs (in 8 patients) out of >2,000 injections

* Injection site reactions includes preferred terms of Injection site reaction, Injection site pain, Injection site erythema, Injection site discolouration, Injection site haemorrhage, and Injection site swelling.

Data on file, Ascendis Pharma 2022.

Open Label Extension (OLE) Efficacy and Safety Results*

- 57 of 57 patients completed the blinded period of ACcomplisH and continued in the OLE on 100 µg/kg/week with 100% retention
- Patients treated ≥6 months at 100 µg/kg/week in the blinded or OLE period demonstrated a consistent and sustained response with mean AHV of 5.39 cm/year (n=40)
- TransCon CNP continued to be well tolerated in the OLE period with safety results consistent with those observed in the blinded period for all patients

Open-label extension data confirms target product profile for once-weekly TransCon CNP 100 µg/kg/week

* Preliminary ACcomplisH Trial live database snapshot as of October 27, 2022.

Data on file, Ascendis Pharma 2022.

Next Steps

- IND submitted for ApproaCH, a global Phase 2b trial in 80 children with achondroplasia aged 2-11; enrollment targeted for completion in early 2023
  - TransCon CNP 100 µg/kg/week vs. Placebo (2:1)
- End of Phase 2 meetings with FDA and EMA planned
- Plan to file IND or similar for TransCon CNP in infants (age 0-2)
- Plan to file IND or similar for a combination trial with TransCon hGH and TransCon CNP
- Expand global reach with finalizing trial in China* and initiating trial in Japan

* Conducted by VISEN Pharmaceuticals.

Thank you

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