SOMATROGON CLINICAL PROGRAM DEVELOPMENT IN Pediatric Growth Hormone Deficiency

Pfizer Rare Disease

Navigation Bar

Top Line Summary

1 Phase 2
2 Phase 2 - OLE
3 Phase 3
4 Phase 3 - OLE
5 Treatment Burden O&E

Somatrogon is indicated in Israel for the treatment of children and adolescents from 3 years of age with growth disturbance due to insufficient secretion of growth hormone

Click on the sections to learn more

SOMATROGON CLINICAL PROGRAM DEVELOPMENT IN pGHD

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Phase 2 CP-4-004

- Study Design
- Endpoints and Criteria

Phase 3 CP-4-006

- Study Design
- Endpoints and Criteria
- Results

Phase 3 Treatment burden O&E

- Study Design
- Endpoints and Criteria
- Results

Phase 2 – OLE CP-4-004-OLE

- Study Design
- Endpoints and Criteria
- Results

Phase 3- OLE CP-4-006-OLE

- Study Design
- Endpoints and Criteria
- Results

Click on the section to learn more

OLE = Open-label extension; pGHD = pediatric growth hormone deficiency

SOMATROGON CLINICAL PROGRAM DEVELOPMENT IN pGHD[1-6]

Phase 2 - CP4-004

- Safety, Efficacy & Dose finding vs Genotropin
- **53** GHD patient
  12 months
- **Naïve** from treatment

Completed

Phase 3 - CP-4-006

- Non-Inferiority to Genotropin
- **224** GHD patient
  12 months
- **Naïve** from treatment

Completed

Treatment Burden O&E

- Cross-over Treatment Burden vs. Genotropin
- **87** GHD patient
  6 months
- **Treatment Experienced**

Completed

CP4-004 - OLE

- Extension
- Safety & Efficacy Study
- 48 GHD patients
- 5 years
- Treatment experienced

Ongoing

CP-4-006 - OLE

- Extension
- Safety & Efficacy Study
- 212 GHD patients
- Treatment experienced

Ongoing

OLE = Open-label extension; pGHD = pediatric growth hormone deficiency

1. Zelinska N, et al. J Clin Endocrinol Metab. 2017;102:1578-1587.2. Zadik et al., Results From an Open-Label Extension of the Phase 2 Dose-Finding Study of Once Weekly Somatrogon vs Daily Genotropin in pGHD, Poster 6887 presented at Endo 2021 3. Deal CL et al, J Clin Endocrinol Metab 2022, 107:e2717-e2728..4.Wajnrajch et al, Switch Data From the Open-Label Extension of the Pivotal Phase 3 Study of Once Weekly Somatrogon Compared With Daily Somatropin in pGHD. Poster 7129 presented at ENDO 2021 5. Horikawa R et al, Phase 3 Study Evaluating Once Weekly Somatrogon Compared to Daily Genotropin in Japanese Patients With pGHD, poster 6600presented at Endo 2021. 6,Maniatis AK et al, Treatment Burden of Weekly Somatrogon vs Daily Somatropin in Children With Growth Hormone Deficiency: A Randomized Study Journal of the Endocrine Society, 2022, 6, 1–10

SAFETY AND DOSE FINDING STUDY OF DIFFERENT SOMATROGON DOSE LEVELS COMPARED TO DAILY GENOTROPIN® THERAPY IN PRE-PUBERTAL GROWTH HORMONE DEFICIENT CHILDREN[1-3]

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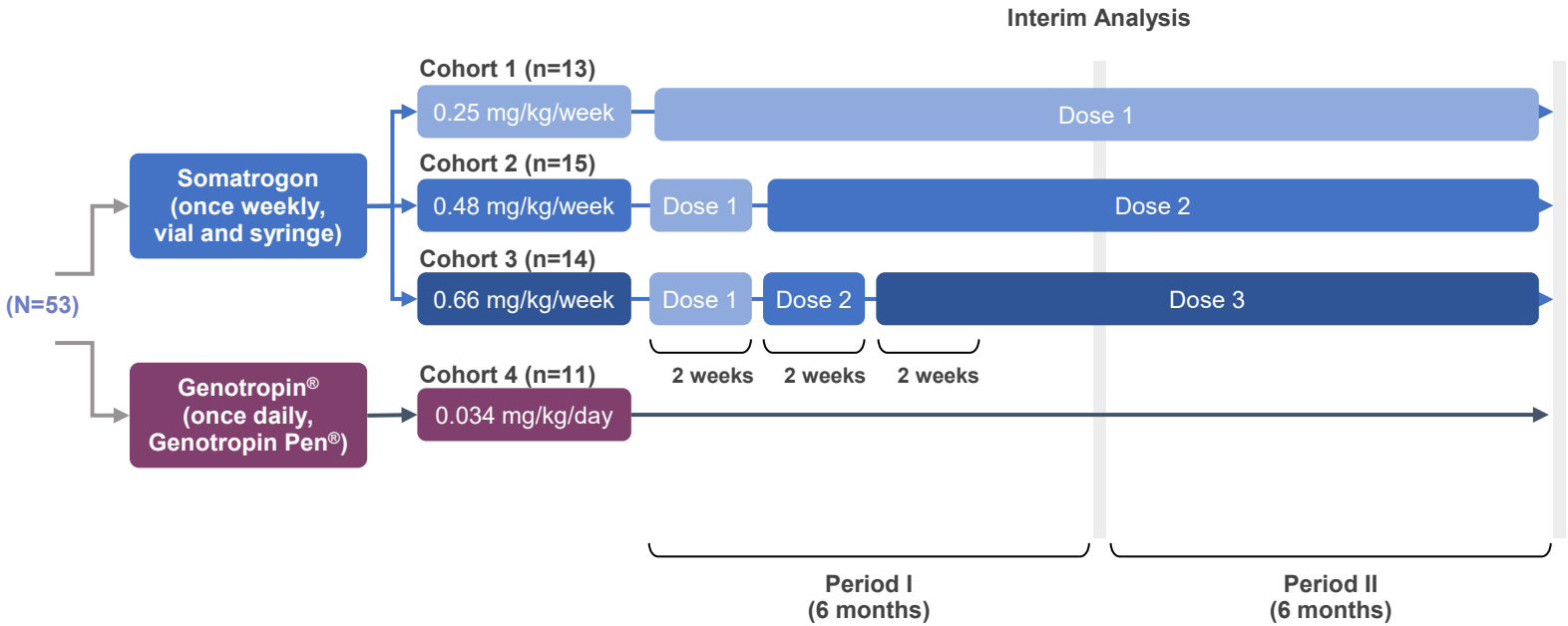
Study Design

Phase II, open label, active-controlled, randomized safety and dose finding study of different somatrogon dose levels compared to daily r-hGH therapy in pre-pubertal growth hormone deficient children.



Key Inclusion Criteria

- Pre-pubertal children aged ≥3 years and < 10 years (girls), or 11 years (boys)
- Isolated GHD or GHD due to multiple pituitary hormone deficiency*
- Peak plasma GH level ≤10 ng/mL on 2 different provocative tests
- Bone age not older than chronological age and < than 9 years (girls) and 10 years (boys)
- Impaired Ht ≤ -2.0 SDS below the mean and annualized HV < -0.7 SDS
- BMI within ±2 SD of mean BMI
- Baseline IGF-1 SDS ≤ -1.0
- Normal karyotype for girls
- No signs or symptoms of intracranial hypertension

Endpoints

Primary Endpoint

- Annual HV at month 12

Secondary Endpoints

- Annualized HV at month 6
- Change in height SDS at months 6 and 12
- Change in IGF-1 SDS

*on stable replacement therapy for ≥3 months, r-hGH= recombinant human Growth hormone, BMI=body mass index; GH=growth hormone; GHD=growth hormone deficiency; Ht=height; HV=height velocity; IGF-1=insulin-like growth factor-1; SDS=standard deviation score.

1 . Zelinska N, et al. J Clin Endocrinol Metab. 2017;102:1578-1587.2 Zadik et al., Results From an Open-Label Extension of the Phase 2. Dose-Finding Study of Once Weekly Somatrogon vs Daily Genotropin in pGHD, Poster 6887 presented at Endo 2021. 3. ClinicalTrials.gov. https://clinicaltrials.gov/ct2/show/study/NCT01592500. Accessed July 18, 2022

SAFETY AND DOSE FINDING STUDY OF DIFFERENT SOMATROGON DOSE LEVELS COMPARED TO DAILY GENOTROPIN® THERAPY IN PRE-PUBERTAL GROWTH HORMONE DEFICIENT CHILDREN[1]

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Results

- **Analyses demonstrated the expected dose dependency**
- **Somatrogon treatment resulted in:**
  - HV comparable to Genotropin®
  - Maintained IGF-1 levels near the ideal standard of 0 SDS
  - Based on both month 12 HV and the IGF-1 profile, Somatrogon 0.66 mg/kg/week was chosen as the dose equivalent to 0.24 mg/kg/week* Genotropin®
- **Somatrogon demonstrated a safety profile similar to Genotropin®**
  - No unexpected AEs
  - Expected AEs were primarily moderate in severity and tended to resolve quickly
  - No patients discontinued or were removed prematurely from the study due to an AE
- **Somatrogon was well tolerated, with the majority of ISRs moderate in severity**
- **ADAs were observed in 6 patients**: 5/42 for Somatrogon group and 1/11 for Genotropin group
  - Antibody titers generally low
  - No associatiation with neutralizing activity or clinical sequelae

* or 0,034mg/kg/day; ISR: Injection site reaction, Ht=height; HV=height velocity; IGF-1=insulin-like growth factor-1; SDS=standard deviation score, ADAs= antidrug antibodies; AEs= Adverse Events

1. Zelinska N, et al. J Clin Endocrinol Metab. 2017;102:1578-1587.

Phase 2-OLE: Design & Endpoints

SAFETY EXTENSION STUDY OF SAFETY AND DOSE FINDING STUDY OF DIFFERENT SOMATROGON DOSE LEVELS COMPARED TO DAILY GENOTROPIN® THERAPY IN PRE-PUBERTAL GROWTH HORMONE DEFICIENT CHILDREN[1-3]

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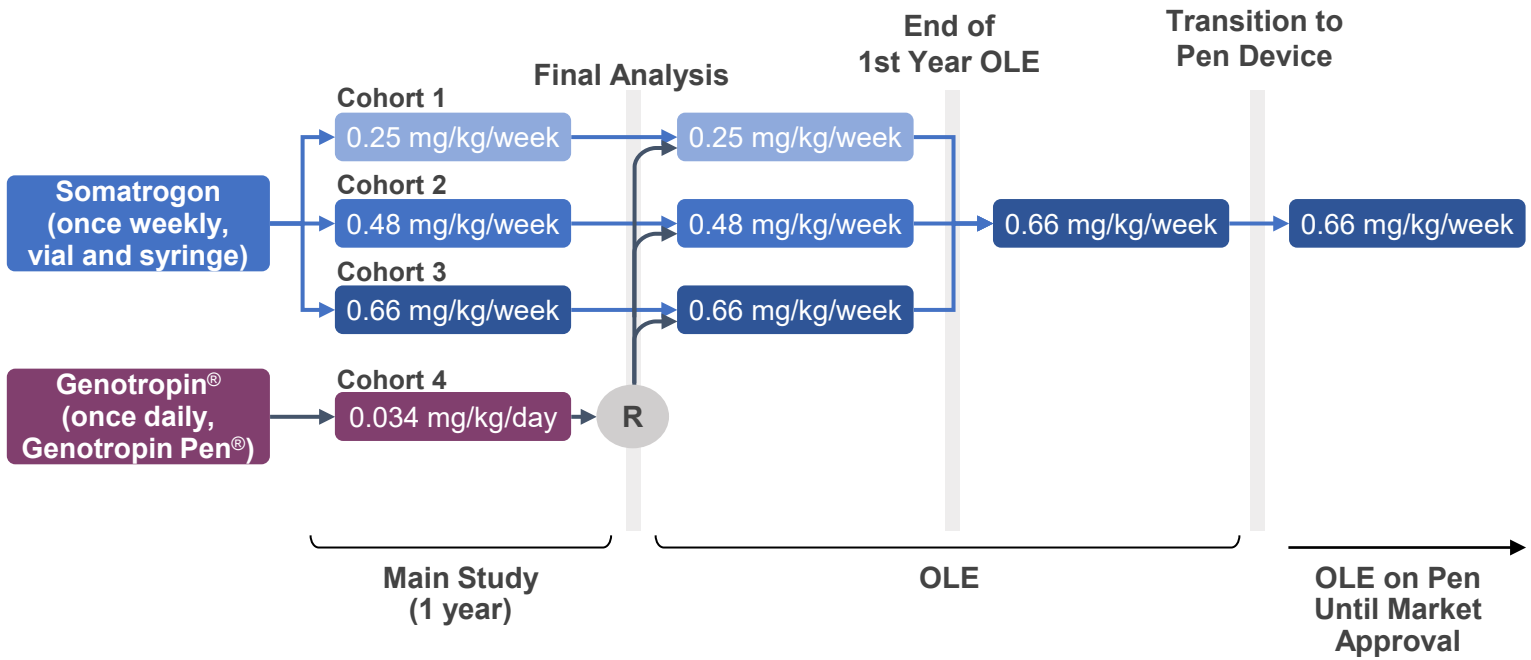
Study Design



Key Inclusion Criteria

Subjects who completed 12 months of treatment in the main study (CP-4-004)

Endpoints

Primary Endpoint

- Safety

Secondary Endpoints

- Annualized HV
- Change in height SDS
- Annual bone maturation

Study Participants

- 48 of 53 subjects who completed the main study were randomized and entered Period III of the OLE.
- At the start of Period III, the majority (66.7%) of subjects were male and almost all (93.8%) of the subjects were White
- Completion rates for each OLE period (Periods III, IV, and Year 1 of Period V) ranged from 87.5 to 97.7%.

*OLE: Safety extension study ,BMI=body mass index; GH=growth hormone; GHD=growth hormone deficiency; Ht=height; HV=height velocity; IGF-1=insulin-like growth factor-1; SDS=standard deviation score.

1. Zelinska N, et al. J Clin Endocrinol Metab. 2017;102:1578-1587. 2. Zadik et al., Results From an Open-Label Extension of the Phase 2 Dose-Finding Study of Once Weekly Somatrogon vs Daily Genotropin in pGHD, Poster 6887 presented at Endo 2021. 3. ClinicalTrials.gov. https://clinicaltrials.gov/ct2/show/study/NCT01592500. Accessed July 18, 2022

SAFETY EXTENSION STUDY OF SAFETY AND DOSE FINDING STUDY OF DIFFERENT SOMATROGON DOSE LEVELS COMPARED TO DAILY GENOTROPIN® THERAPY IN PRE-PUBERTAL GROWTH HORMONE DEFICIENT CHILDREN[1]

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Results

- Subjects treated with Somatrogon for up to 5 years showed sustained improvement in clinical parameters of growth, including annual HV, change in height SDS, and height SDS
- Somatrogon demonstrated safety and tolerability, with no ISRs reported during use of the vial and 3 mild to moderate ISRs reported while using the pen device
- IGF-1 SDS values were maintained within the normal range
- No clinically meaningful differences were observed between ADA-positive and ADA-negative subjects

ISR: Injection site reaction, Ht=height; HV=height velocity; IGF-1=insulin-like growth factor-1; SDS=standard deviation score

1.Zadik et al., Results From an Open-Label Extension of the Phase 2 Dose-Finding Study of Once Weekly Somatrogon vs Daily Genotropin in pGHD, Poster 6887 presented at Endo 2021.

SAFETY AND EFFICACY NON-INFERIORITY TO GENOTROPIN® PHASE 3 STUDY OF SOMATROGON IN GROWTH HORMONE DEFICIENT CHILDREN[1,2]

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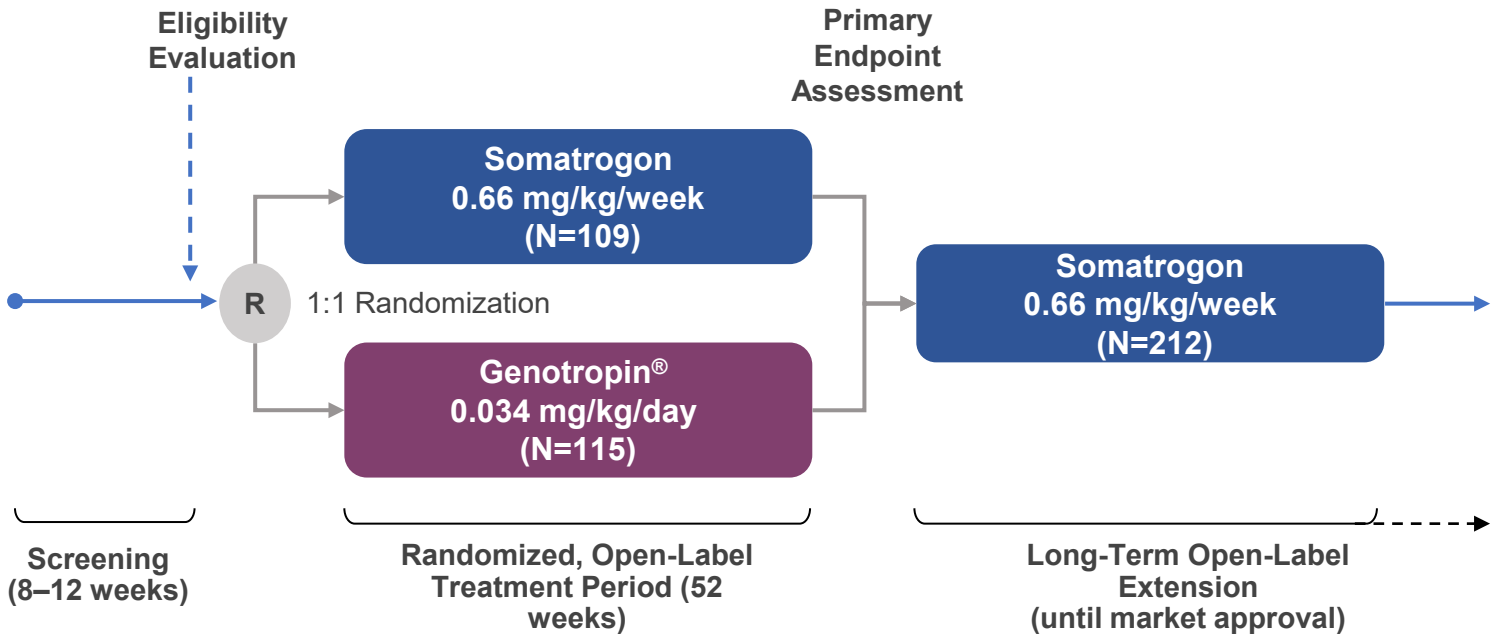
Study Design

Phase III, randomized, safety and efficacy non-inferiority to Genotropin® study of Somatrogon in Growth Hormone deficient children.



Key Inclusion Criteria

- GH treatment–naive pre-pubertal children with GHD
- Age ≥3 years and ≤ 10 years (girls), ≤ 11 years (boys)
- Peak plasma GH level ≤10 ng/mL on 2 different provocative tests
- Bone age not older than chronological age <10 years (girls), <11 years (boys)
- Normal karyotype for girls
- Annualized HV SDS < -0.7 (< 25th percentile for chronological age)
- IGF-1 SDS ≤ -1.0

Endpoints

Primary Endpoint

- Annual HV at month 12

Secondary Endpoints

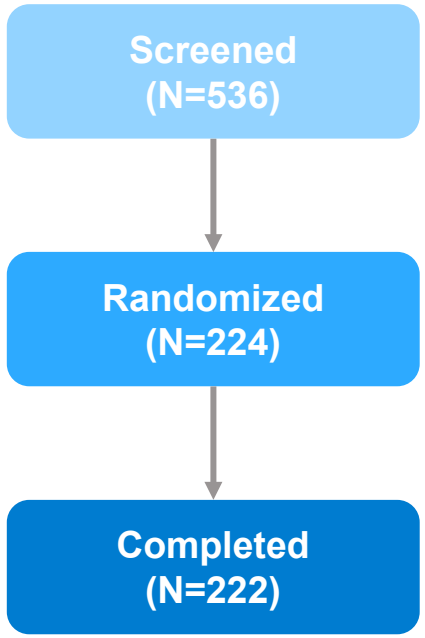
- Annualized HV at month 6
- Change in height SDS at months 6 and 12
- Change in bone maturation at month 12*

* annual change in bone age measurements per Greulich-Pyle method,BMI=body mass index; GH=growth hormone; GHD=growth hormone deficiency; Ht=height; HV=height velocity; score, ; IGF-1=insulin-like growth factor-1; IGFB=insulin-like factor-binding protein; SDS=standard deviation score.

1. Deal CL et al, J Clin Endocrinol Metab 2022, 107:e2717-e2728. 2. https://clinicaltrials.gov/ct2/show/NCT02968004?term=NCT02968004&draw=2&rank=1 Accessed July 18, 2022

SAFETY AND EFFICACY NON-INFERIORITY TO GENOTROPIN® PHASE 3 STUDY OF SOMATROGON IN GROWTH HORMONE DEFICIENT CHILDREN[1]

	Somatrogon (N=109)	Genotropin® (N=115)
Age (years), mean (SD)	7.83 (2.66)	7.61 (2.37)
Male, n (%)	82 (75.2)	79 (68.7)
Race, n (%)		
White	81 (74.3)	86 (74.8)
Asian	24 (22.0)	21 (18.3)
Other	4 (3.7)	8 (6.9)
Peak GH level, n (%)		
≤3 ng/mL	22 (20.2)	21 (18.3)
>3 ng/mL and ≤7 ng/mL	53 (48.6)	56 (48.7)
>7 ng/mL and <10 ng/mL	34 (31.2)	38 (33.0)
HT SDS, mean (SD)	-2.94 (1.29)	-2.78 (1.27)



- Somatrogon, n= 108
- Genotropin®, n= 114

IGF-1=insulin-like growth factor-1; SDS=standard deviation score.

1. Deal CL et al, J Clin Endocrinol Metab 2022, 107:e2717-e2728.

SAFETY AND EFFICACY NON-INFERIORITY TO GENOTROPIN® PHASE 3 STUDY OF SOMATROGON IN GROWTH HORMONE DEFICIENT CHILDREN[1]

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Results[1]

- **The study met the primary objective of non-inferiority of somatrogon compared with Genotropin®**
  - Annual HV at month 12 for somatrogon was numerically higher in comparison to Genotropin®
  - Change in height SDS and various sensitivity analyses for the primary endpoint* were numerically higher for somatrogon group compared with Genotropin® group
- Over 95% of the patients achieved estimated mean insulin-like growth factor-1 SDS levels within the normal range of ±2 SDS
- **Low numbers of serious adverse events were reported in both the somatrogon and Genotropin® groups**
  - The majority of adverse events were mild to moderate in severity
- **Somatrogon administration was generally well tolerated in pediatric patients with growth hormone deficiency**

* including the use of observed data, and subgroup analyses; IGF-1=insulin-like growth factor-1; SDS=standard deviation score, HV= Height Velocity,

1. Deal CL et al, J Clin Endocrinol Metab 2022, 107:e2717-e2728.

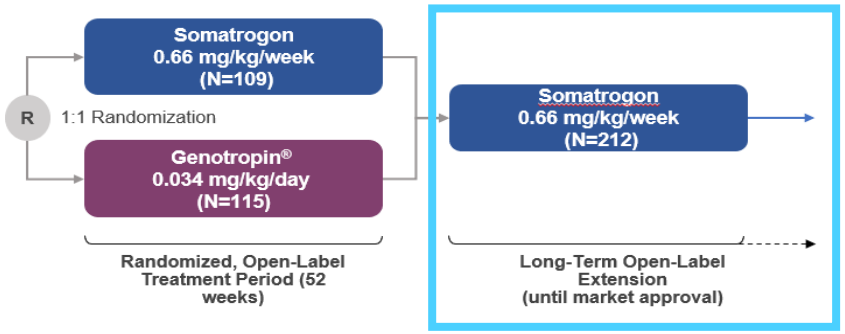
OPEN-LABEL EXTENSION PHASE 3 STUDY CONTINUATION OF THE RANDOMIZED 12-MONTH MAIN STUDY[1]

Study Design

- **Open-label,** single arm, extension phase 3 study continuation of the randomized 12-month main study

Dosing

- Subjects who received somatrogon during the main study continued with the same dose during the OLE
- Subjects who received Genotropin® during the main study were switched to somatrogon and began treatment with a dose of 0.66 mg/kg/week
- The dose of somatrogon can be adjusted every 3 months based on the subject's body weight and may be decreased for safety reasons based on predefined dose-adjustment criteria



Key Inclusion Criteria

Subjects who completed the main study and provided their consent were eligible to be enrolled

Endpoints

- Annual HV, change in height SDS, bone maturation
- IGF-1 levels, IGF-1 SDS, IGFBP-3 levels, and IGFBP-3 SDS, assessed on Day 4 after Somatrogon dosing across study visits.

Study Participants

- 212 subjects completed the main study and enrolled over to OLE
  - Somatrogon, n= 104
  - Genotropin, n=108.

AE=adverse event; IGF-1=insulin-like growth factor-1; IGFBP-3=Insulin Like growth factor binding protein-3; OLE=open-label extension; SDS=standard deviation score, HV= Height velocity.

1.Wajnrajch et al, Switch Data From the Open-Label Extension of the Pivotal Phase 3 Study of Once Weekly Somatrogon Compared With Daily Somatropin in pGHD. Poster 7129 presented at ENDO 2021

PHASE 3 OPEN-LABEL, MULTI-CENTER, 2-PERIOD CROSSOVER STUDY TO DEMONSTRATE REDUCTION IN TREATMENT BURDEN WITH SOMATROGON COMPARED TO GENOTROPIN®[1,2]

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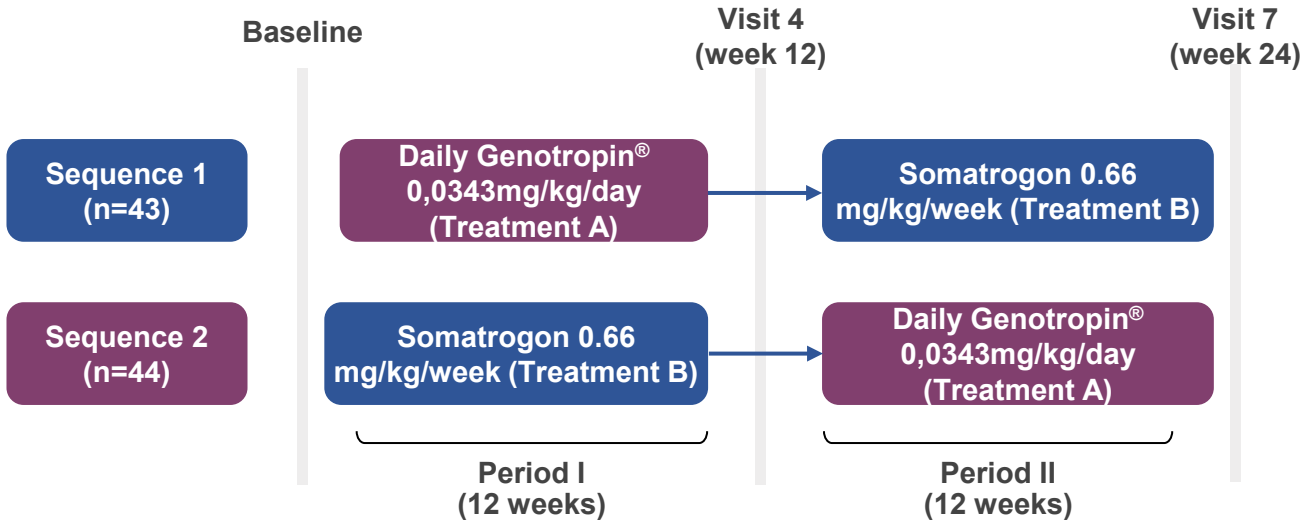
Study Design

- **Phase III**, open-label, multi-center, 2-period crossover study to demonstrate reduction in treatment burden with Somatrogon compared to Genotropin®.
- Already treated patient by r-hGH



Key Inclusion Criteria

- Children aged 3 years to <18 years
- Isolated GHD or GHI
- Currently on treatment with Genotropin Pen®, Genotropin GoQuick Pen®, HumatroPen®, or Omnitrope® Pen ≥3 months and compliant on a stable dose (±10%) for ≥3 months, prior to screening
- IGF-1 SDS <2
- Optimized and stable treatment for other hypothalamic-pituitary axis hormonal deficiencies and/or diabetes insidipus, for ≥3 months prior to screening

Endpoints

Primary Endpoint

- Treatment burden* total scores between weekly injection schedule and daily injection schedule

Secondary Endpoints

- Pen ease of use
- Ease and convenience of the injection schedule
- Satisfaction with overall treatment experience
- Willingness to continue injection schedule
- Patient-reported injection signs and symptoms (≥8 years of age)

*life interference; rh-GH= recombinant human growth hormone; GHD= Growth hormone Deficiency, GHI= Growth Hormone Insufficiency; IGF-1= Insulin-like growth factor-1, SDS= standard deviation score

1. ClinicalTrials.gov. https://clinicaltrials.gov/ct2/show/NCT03831880. Accessed September July 18, 2022. 2. Maniatis AK et al, Treatment Burden of Weekly Somatrogon vs Daily Somatropin in Children With Growth Hormone Deficiency: A Randomized Study Journal of the Endocrine Society, 2022, 6, 1–10

PHASE 3 OPEN-LABEL, MULTI-CENTER, 2-PERIOD CROSSOVER STUDY TO DEMONSTRATE REDUCTION IN TREATMENT BURDEN WITH SOMATROGON COMPARED TO GENOTROPIN®[1]

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Results

- **Compared with once daily Genotropin, Somatrogon administered once weekly**
  - has a lower treatment burden as shown by less life interference
  - is associated with a more favorable treatment experience.

- **No severe or serious adverse events were reported during somatrogon or Genotropin® treatment.**
  - One subject discontinued study drug during treatment with somatrogon due to an adverse events
  - Injection site pain was the most common TEAE during treatment with Genotropin (12.8%) and somatrogon (14.9%) and was rated as mild in most cases

- All adverse events were mild to moderate in severity

TEAE = Treatment emergent adverse event

1 Maniatis AK et al, Treatment Burden of Weekly Somatrogon vs Daily Somatropin in Children With Growth Hormone Deficiency: A Randomized Study Journal of the Endocrine Society, 2022, 6, 1–10

SOMATROGON CLINICAL PROGRAM DEVELOPMENT IN Pediatric Growth Hormone Deficiency

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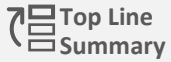
Navigation Bar



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