Ascendis Pharma A/S

YORVIPATH® FDA Approval

August 12, 2024

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 expected timing of U.S. commercial launch and product shipments for YORVIPATH; our expectations regarding the potential benefits of YORVIPATH; our U.S. launch plans for YORVIPATH; the potential market size and size of the potential patient populations for YORVIPATH; our patient services for YORVIPATH; the cost of YORVIPATH; our Vision 2030; plans and objectives of management for future operations and commercialization activities; and future results of current and anticipated products and product candidates 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 (SEC), including, without limitation, our most recent Annual Report on Form 20-F filed with the SEC on February 7, 2024 particularly in the sections titled “Risk Factors” and “Operating and Financial Review and Prospects.” 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.

YORVIPATH has been approved by the U.S. Food and Drug Administration for the treatment of hypoparathyroidism in adults. In the EU, Norway, Iceland, and Great Britain, YORVIPATH has also been granted marketing authorization as a once-daily subcutaneous injection for the treatment of adults with chronic hypoparathyroidism. YORVIPATH is and has been under clinical investigation and has not yet been approved for marketing by other foreign regulatory authorities.

YORVIPATH® Now FDA Approved

Yorvipath®
palopegteriparatide

- YORVIPATH is the first and only FDA-approved product for the treatment of hypoparathyroidism in adults[1]
- Second FDA-approved product utilizing TransCon® technology

[1] Limitations of Use: YORVIPATH was not studied for acute post-surgical hypoparathyroidism. YORVIPATH's titration scheme was only evaluated in adults who first achieved an albumin-corrected serum calcium of at least 7.8 mg/dL using calcium and active vitamin D treatment. YORVIPATH [package insert]. Princeton, NJ: Ascendis Pharma Endocrinology, Inc. August 2024.

ascendis pharma

Key YORVIPATH Takeaways

- Indicated for the treatment of hypoparathyroidism in adults[1]
- No REMS / black box
- Post Marketing Requirements
  - Clinical lactation study
  - Pregnancy safety study
- Transitioning to YORVIPATH U.S. commercial activity
  - Ascendis team has been preparing to launch since 2023
  - Market access teams now engaging payers with approved label
  - U.S. product availability expected Q1 2025; plan to request FDA approval to commercialize existing manufactured product, which, if approved, could be introduced in the U.S. in Q4 2024

[1] Limitations of Use: YORVIPATH was not studied for acute post-surgical hypoparathyroidism. YORVIPATH's titration scheme was only evaluated in adults who first achieved an albumin-corrected serum calcium of at least 7.8 mg/dL using calcium and active vitamin D treatment. YORVIPATH [package insert]. Princeton, NJ: Ascendis Pharma Endocrinology, Inc. August 2024.

YORVIPATH: Select Highlights of U.S. Prescribing Information

INDICATIONS AND USAGE

YORVIPATH is indicated for the treatment of hypoparathyroidism in adults.

Limitations of Use:
- Not studied for acute post-surgical hypoparathyroidism.
- Titration scheme only evaluated in adults who first achieved an albumin-corrected serum calcium of at least 7.8 mg/dL using calcium and active vitamin D treatment.

DOSAGE AND ADMINISTRATION

- Use only one injection to achieve the once daily recommended dosage.
- Maximum recommended YORVIPATH dosage is 30 mcg subcutaneously once daily.
- Individualize YORVIPATH dosage based on serum calcium.
- Refer to the Full Prescribing Information for complete dosage and administration information.

SAFETY

Contraindications
Severe hypersensitivity to palopegteriparatide or any components of YORVIPATH

Warnings and Precautions
- Unintended changes in serum calcium levels related to number of daily injections
- Serious hypercalcemia and hypocalcemia
- Potential risk of osteosarcoma
- Orthostatic hypotension
- Digoxin toxicity

Adverse reactions occurring in ≥5% of patients
Injection site reactions, vasodilatory signs and symptoms, headache, diarrhea, back pain, hypercalcemia, and oropharyngeal pain.

YORVIPATH® [package insert]. Princeton, NJ: Ascendis Pharma Endocrinology, Inc. August 2024.

Two TransCon Products Now Approved in Major Markets

TransCon hGH

- Pediatric Growth Hormone Deficiency[1]

Skytrofa® lonapegsomatropin-tcgd

- **United States**[2]
  Approved in the U.S. as SKYTROFA® (lonapegsomatropin-tcgd)
- **European Union**[3] **and Selected Other Countries**[4]
  Approved in the EU as SKYTROFA (lonapegsomatropin)

TransCon PTH

- Hypoparathyroidism in adults[8]

Yorvipath® palopegteriparatide

- **United States**[5]
  Approved in the U.S. as YORVIPATH (palopegteriparatide)
- **European Union**[6] **and Selected Other Countries**[7]
  Approved in the EU as YORVIPATH (palopegteriparatide)

[1] In the U.S., SKYTROFA is 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. In the EU, the therapeutic indication for SKYTROFA is growth failure in children and adolescents aged from 3 years up to 18 years due to insufficient endogenous growth hormone secretion (growth hormone deficiency [GHD]).
[2] SKYTROFA [package insert]. Princeton, NJ: Ascendis Pharma Endocrinology, Inc. October 2022.
[3] SKYTROFA SmPC. Hellerup, Denmark: Ascendis Pharma Endocrinology Division A/S. October 2023.
[4] SKYTROFA is also approved in Norway, Iceland, Lichtenstein and Great Britain (covering England, Wales, Scotland).
[5] YORVIPATH [package insert]. Princeton, NJ: Ascendis Pharma Endocrinology, Inc. August 2024.
[6] YORVIPATH SmPC. Hellerup, Denmark: Ascendis Pharma Bone Diseases A/S. November 2023.
[7] YORVIPATH is also approved in Norway, Iceland and Great Britain (covering England, Wales, Scotland).
[8] In the U.S., YORVIPATH is indicated for the treatment of hypoparathyroidism in adults. In the EU, the therapeutic indication for YORVIPATH is a parathyroid hormone (PTH) replacement therapy indicated for the treatment of adults with chronic hypoparathyroidism.

Vision 2030

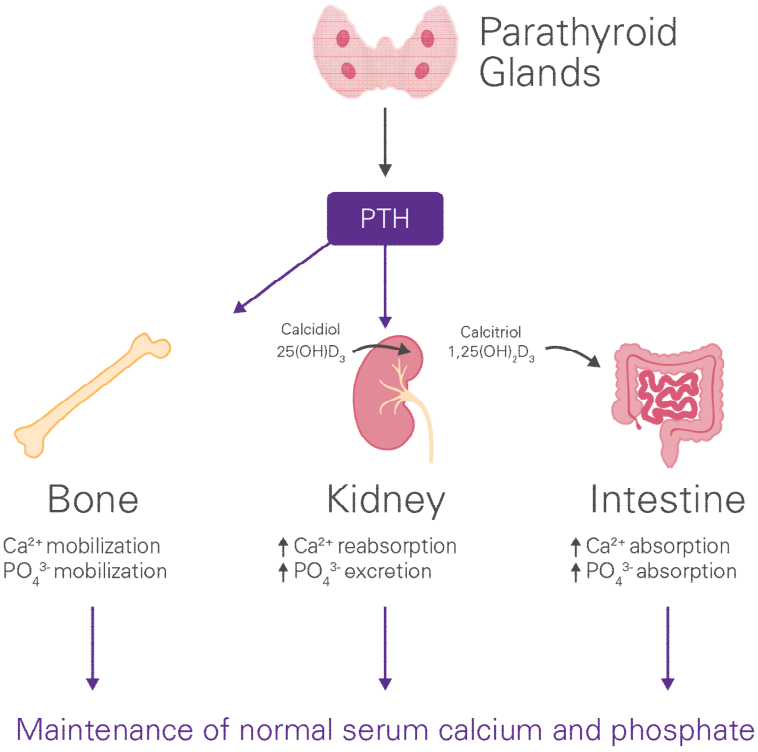
Achieve blockbuster status for multiple products and expand our engine for future innovation

- **Be the Leading Endocrinology Rare Disease Company**
  - Achieve blockbuster status (>$1B) for TransCon PTH, TransCon hGH, and TransCon CNP through worldwide commercialization
  - Be the leader in Growth Disorders and Hypoparathyroidism, pursuing clinical conditions, innovative LCM and complementary patient offerings
  - Expand pipeline with Endocrinology Rare Disease blockbuster product opportunities
- **Create Value in Additional Therapeutic Areas through Innovative Business Models**
  - Obtain accelerated approval in oncology with registrational trials ongoing
  - Pursue TransCon product opportunities in >$5B indications
  - Maximize value creation of these product opportunities through collaboration with therapeutic area market leaders
- **Differentiate with Ascendis Fundamentals**
  - Outperform industry drug development benchmarks with Ascendis' product innovation algorithm
  - Remain independent as a profitable biopharma through lean and flexible ways of working
  - Let our values Patients, Science, Passion drive our decisions to success

Hypoparathyroidism: An Unmet Medical Need

PTH Therapy for Hypoparathyroidism

- An intact PTH axis maintains normal serum calcium and phosphate homeostasis[1,2,3]
- PTH promotes normal nerve and muscle function[4]
- Conventional therapy for hypoparathyroidism (active vitamin D [e.g., calcitriol], and oral calcium) aims to alleviate hypocalcemic symptoms but fails to replicate normal PTH physiology
- The theoretical advantages of PTH over conventional therapy in the management of hypoparathyroidism include:[5]
  - a reduction in the amounts of calcium and vitamin D requirements,
  - reduction in urinary calcium,
  - improvement in quality of life,
  - reduction in ectopic soft tissue calcification, and
  - improvement in abnormal bone remodeling dynamics

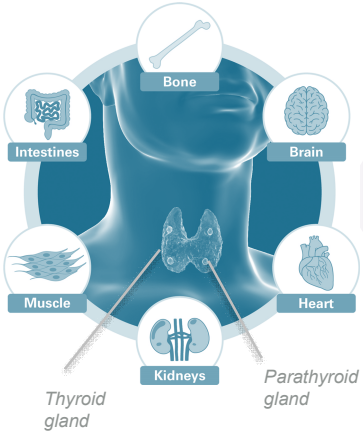


PTH, parathyroid hormone.

1. Khan AA, et al. *J Bone Miner Res*. 2022;37:2568-2585. 2. Shoback DM, et al. *J Clin Endocrinol Metab*. 2016;101(6):2300-2312. 3. Bilezikian JP, et al. *J Clin Endocrinol Metab*. 2016;101(6):2313-2324. 4. Mannstadt M, et al. *Nat Rev Dis Primers*. 2017; 3:17055. 5. Cusano NE, et al. *Best Pract Res Clin Endocrinol Metab*. 2015;29(1):47-55.

Hypoparathyroidism: One Disease, Multiple Consequences[1-4]

Absence or deficiency of parathyroid hormone (PTH) is linked to multi-organ manifestations.[5,6]



CENTRAL NERVOUS SYSTEM
- Seizures
- Basal ganglia calcifications
- Parkinsonism or dystonia

RESPIRATORY
- Laryngospasm

CARDIOVASCULAR
- Vascular calcifications
- Cardiac arrhythmias
- Hypocalcemia-associated dilated cardiomyopathy

RENAL
- Nephrocalcinosis*
- Nephrolithiasis*
- Chronic kidney disease*

PERIPHERAL NERVOUS SYSTEM
- Paresthesia
- Muscle cramps
- Pain
- Tetany

NEUROPSYCHIATRIC
- Anxiety & depression
- Cognitive impairment ("brain fog")

OPHTHALMALOGICAL
- Cataracts
- Papilledema

DENTAL
- Altered tooth morphology

DERMATOLOGICAL
- Dry skin
- Thinning hair
- Brittle nails

MUSCULOSKELETAL
- Myopathy
- Spondyloarthropathy

Despite treatment with conventional therapy, patients report impairments in quality of life[7]

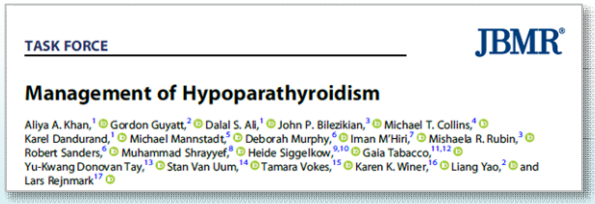
* These manifestations are mostly the result of management with calcium and active vitamin D, rather than of the disease itself.

1. Underbjerg L, Sikjaer T, Mosekilde L, et al. *J Bone Miner Res.* 2013;28(11):2277-2285. **2.** Underbjerg L, Sikjaer T, Mosekilde L, et al. *J Bone Miner Res.* 2015;30(9):1738-1744. **3.** Shoback DM, Bilezikian JP, Costa AG, et al. *J Clin Endocrinol Metab.* 2016;101(6):2300-2312. **4.** Underbjerg L, Sikjaer T, Mosekilde L, et al. *J Bone Miner Res.* 2015;30(9):1738-1744. **5.** Mannstadt M, Bilezikian JP, Thakker RV, et al. *Nat Rev Dis Primers.* 2017;3:17055. **6.** Shoback DM, Bilezikian JP, Costa AG, et al. *J Clin Endocrinol Metab.* 2016;101(6):2300-2312. **7.** Büttner, M., Singer, S. & Taylor, K. *Endocrine* (2024).

ascendis pharma

Latest Clinical Practice Guideline[1]

- Consider PTH replacement therapy in patients not adequately controlled on conventional therapy
- Inadequate control is considered to be <u>any one</u> of the following:
  - Symptomatic hypocalcemia
  - Hyperphosphatemia
  - Renal insufficiency
  - Hypercalciuria
  - Poor quality of life
- In addition, individuals with poor compliance, malabsorption, or who are intolerant of large doses of calcium and active vitamin D may also benefit from PTH replacement therapy


TASK FORCE

JBMR®

Management of Hypoparathyroidism

Aliya A. Khan,[1] Gordon Guyatt,[2] Dalal S. Ali,[1] John P. Bilezikian,[3] Michael T. Collins,[4] Karel Dandurand,[1] Michael Mannstadt,[5] Deborah Murphy,[6] Iman M'Hiri,[7] Mishaela R. Rubin,[3] Robert Sanders,[8] Muhammad Shrayyef,[8] Heide Siggelkow,[9,10] Gaia Tabacco,[11,12] Yu-Kwang Donovan Tay,[13] Stan Van Uum,[14] Tamara Vokes,[15] Karen K. Winer,[16] Liang Yao,[2] and Lars Rejnmark[17]

1. Khan AA, et al. *J Bone Miner Res*. 2022;37:2568-2585.

YORVIPATH U.S. Label: Efficacy and Safety

Efficacy at Week 26 in Adults with Hypoparathyroidism

	YORVIPATH (N=61)	Placebo (N=21)	Response Rate Difference (95% CI)
Overall Response at Week 26	42 (68.9%)	1 (4.8%)	64.2% (49.5%, 78.8%)
Response for each component			
Normal albumin-corrected serum calcium[a]	49 (80.3%)	10 (47.6%)	32.7% (9.2%, 56.3%)
Independence from active vitamin D[b]	58 (95.1%)	5 (23.8%)	71.3% (52.5%, 90.2%)
Independence from therapeutic dose of calcium[c]	53 (86.9%)	1 (4.8%)	82.2% (70.0%, 94.4%)
No increase in study drug dose since Week 22[d]	57 (93.4%)	12 (57.1%)	36.4% (14.2%, 58.5%)
Study drug dose ≤30 mcg/day up to Week 26[e]	56 (91.8%)	NA	NA

[a] Normal range for albumin-corrected serum calcium was 8.3 to 10.6 mg/dL.
[b] No daily standing doses of active vitamin D, no PRN doses, and no missing active vitamin D data within 4 weeks prior to Week 26 visit.
[c] Average daily standing dose of elemental calcium ≤600 mg, no PRN doses, and no missing calcium data within 4 weeks prior to Week 26 visit.
[d] No increase in study drug dose within 4 weeks prior to Week 26 visit.
[e] Subjects who received more than 30 mcg/day at any timepoint during the 26-week treatment period were considered as non-responders for the efficacy endpoint.
Abbreviations: CI: confidence interval; NA: not applicable; PRN: pro re nata.

YORVIPATH [package insert]. Princeton, NJ: Ascendis Pharma Endocrinology, Inc. August 2024.

Adverse Reactions in ≥5% of Subjects with Hypoparathyroidism Treated with YORVIPATH and with ≥2% Higher Frequency Compared to Placebo

Adverse Reaction	YORVIPATH (N = 61) n (%)	Placebo (N = 21) n (%)
Injection site reactions[a]	24 (39)	1 (5)
Vasodilatory signs and symptoms[b]	17 (28)	0 (0)
Headache	13 (21)	2 (10)
Diarrhea	6 (10)	1 (5)
Back pain[c]	5 (8)	0 (0)
Hypercalcemia	5 (8)	0 (0)
Oropharyngeal pain	4 (7)	0 (0)

[a] Injection site reactions includes the preferred terms injection site bruising, injection site erythema, injection site rash, and injection site reaction.
[b] Vasodilatory signs and symptoms includes the preferred terms blood pressure orthostatic decreased, dizziness, dizziness postural, orthostatic hypotension, palpitations, postural orthostatic tachycardia syndrome, presyncope, syncope, and vertigo.
[c] Back pain includes the preferred terms back pain, flank pain, and spinal pain.
Abbreviations: N, total number of subjects in the treatment arm; n, number of subjects with the adverse reaction; %, percent of subjects with the adverse reaction.

YORVIPATH [package insert]. Princeton, NJ: Ascendis Pharma Endocrinology, Inc. August 2024.

U.S. Launch Plan

Hypoparathyroidism: Significant U.S. Patient Population

PTH Experienced

~4,000–5,000[2]

- Patients previously treated with PTH

Total US Prevalence

70,000–90,000[1,3]

- Currently treated with active vitamin D and calcium

Newly Diagnosed

~3,000[3] annually

- Post-surgical, auto-immune, genetic, or idiopathic

We estimate ~90% of patients with hypoparathyroidism have insurance coverage[4]

1. U.S. prevalence literature review (Powers, Clarke).
2. Internal estimates and Symphony Metys data.
3. U.S. prevalence literature review and epi meta-analysis (Powers, Clarke, Milliman project, ipm.ai claims project; HCUPnet, Healthcare Cost and Utilization Project. Agency for Healthcare Research and Quality, Rockville, MD for surgical cohort projection).
4. The percentage of people with health insurance coverage for all or part of 2022 was 92.1% (www.census.gov).

Transitioning to YORVIPATH Commercial Activity

Key launch initiatives focus on awareness and education…

- Multi-channel disease education and product awareness campaign
- Outreach to key national and regional opinion leaders
- Showcasing YORVIPATH at key fall congress meetings*

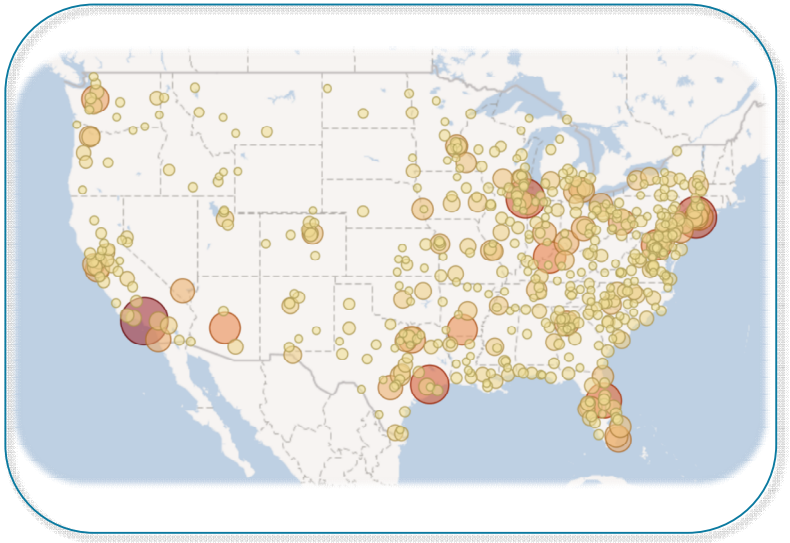
…leveraging established endocrine rare disease commercial infrastructure

- Established payer engagement with expanded endocrine portfolio
- Build upon the robust foundation of patient support
- Leverage commercial operations and analytics framework

U.S. product availability expected Q1 2025; plan to request FDA approval to commercialize existing manufactured product

*American Society of Bone and Mineral Research (ASBMR), and American Thyroid Association (ATA)

Targeted approach covering ~80% of the opportunity

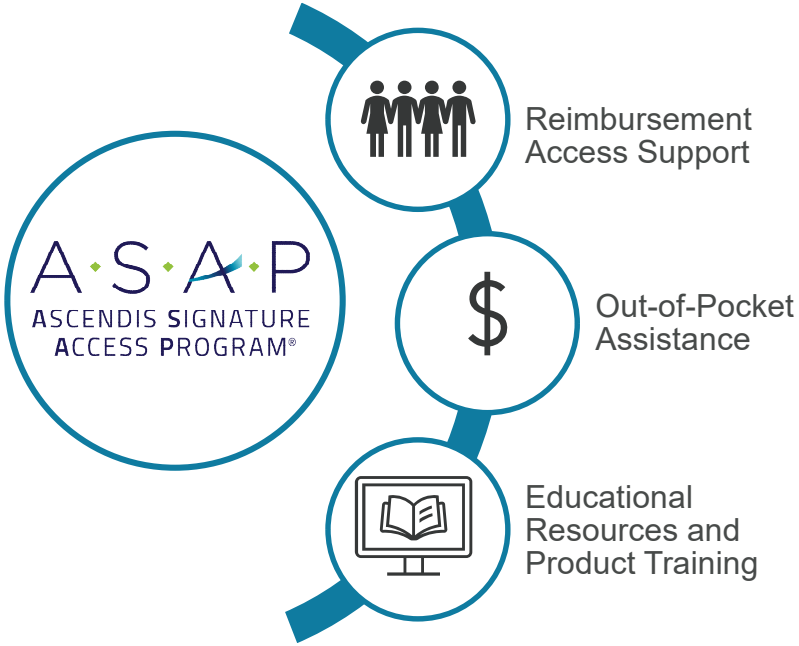


- ~6,000 HCPs Actively involved with diagnosing and treating patients[1]
- Majority of targets in endocrinology and represent ~80% of opportunity[1]
- Experienced commercial team with expertise in specialty products and rare disease markets

1. Based on Symphony Claims data.

Ensuring Patients Have Affordable and Broad Access to YORVIPATH

Patient Access



Cost to Patient

- **Commercial:** Eligible commercially insured patients pay as little as $5 a month with a co-pay card
- **Government:** Affordable out-of-pocket or patients will be screened for available assistance programs
- **Uninsured or underinsured:** Patients who require additional assistance will be screened for the Ascendis Patient Assistance Program (PAP)

Summary & Next Steps

- YORVIPATH is the first and only FDA-approved product for the treatment of hypoparathyroidism in adults[1]
- Hypoparathyroidism patient and physician community aware & engaged
- Transitioning to YORVIPATH U.S. commercial activity
- Request FDA approval to commercialize existing manufactured product, which, if approved, could be introduced in the U.S. in the fourth quarter of 2024
- Second Ascendis Endocrine Rare Disease product being launched in a multi-billion-dollar U.S. market opportunity[2]

Building the leading Endocrinology Rare Disease company

[1] Limitations of Use: YORVIPATH was not studied for acute post-surgical hypoparathyroidism. YORVIPATH's titration scheme was only evaluated in adults who first achieved an albumin-corrected serum calcium of at least 7.8 mg/dL using calcium and active vitamin D treatment. YORVIPATH [package insert]. Princeton, NJ: Ascendis Pharma Endocrinology, Inc. August 2024.
[2] Ascendis internal estimate.