***XHANCE is a corticosteroid indicated for the treatment of nasal polyps in patients 18 years of age or older.***

XHANCE® (fluticasone propionate) nasal spray 93 mcg

# Are your patients suffering from congestion despite use of conventional intranasal steroid sprays?

## When nasal polyp symptoms persist... it may be time for XHANCE.

**IMPORTANT SAFETY INFORMATION**

**CONTRAINDICATIONS:** Hypersensitivity to any ingredient in XHANCE.

**WARNINGS AND PRECAUTIONS:**

- Local Nasal Effects: epistaxis, erosion, ulceration, septal perforation, *Candida albicans* infection, and impaired wound healing. Monitor patients periodically for signs of possible changes on the nasal mucosa. Avoid use in patients with recent nasal ulcerations, nasal surgery, or nasal trauma.

**Please see additional Important Safety Information on page 13.**

# Maximize medical management of XHANCE

XHANCE is a corticosteroid indicated for the treatment of nasal polyps in patients 18 years of age or older

**When patients remain symptomatic after conventional intranasal steroids, choose XHANCE next in a stepped-care approach to treat nasal polyps[1,2]**


**Evidence supports use of XHANCE. It's time.[3,4]**

– Differentiated from conventional nasal sprays—XHANCE uses an Exhalation Delivery System that reaches high and deep in the nasal passages where nasal polyps originate[1,3,4]

– XHANCE is included as a treatment option distinct from conventional intranasal steroids as part of the ACAAI/ARS shared decision model[2]

***When symptoms persist, reach high and deep with XHANCE.***

**IMPORTANT SAFETY INFORMATION**

**WARNINGS AND PRECAUTIONS (continued):**

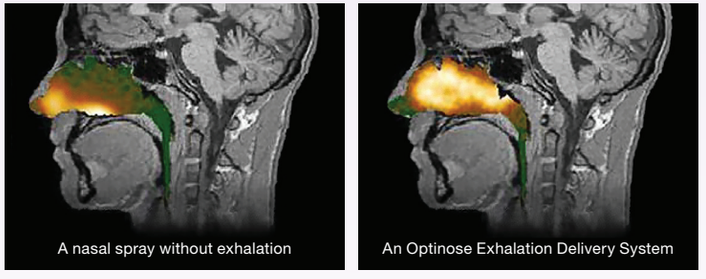
- Close monitoring for glaucoma and cataracts is warranted.
- Hypersensitivity reactions (e.g., anaphylaxis, angioedema, urticaria, contact dermatitis, rash, hypotension, and bronchospasm) have been reported after administration of fluticasone propionate. Discontinue XHANCE if such reactions occur.



# XHANCE helps deliver medication high and deep

**Deposition is different with an Exhalation Delivery System (EDS)[5]**

**Deposition demonstrated through gamma scintigraphy[5]**




Gamma camera images after using a nasal spray without exhalation (left) and an Optinose® Exhalation Delivery System with exhalation (right). The images are from healthy subjects taken 2 minutes after administration with radiolabeled solution and are representative of the overall findings from 211 images and 56 subjects.

**The clinical relevance of different deposition patterns has not been established.**

- Conventional nasal steroid sprays deposit drug predominantly in the inferior and anterior parts of the nasal cavity[6-8]

**IMPORTANT SAFETY INFORMATION**

**WARNINGS AND PRECAUTIONS (continued):**

- Immunosuppression: potential increased susceptibility to or worsening of infections (e.g., existing tuberculosis; fungal, bacterial, viral, or parasitic infection; ocular herpes simplex). Use with caution in patients with these infections. More serious or even fatal course of chickenpox or measles can occur in susceptible patients.

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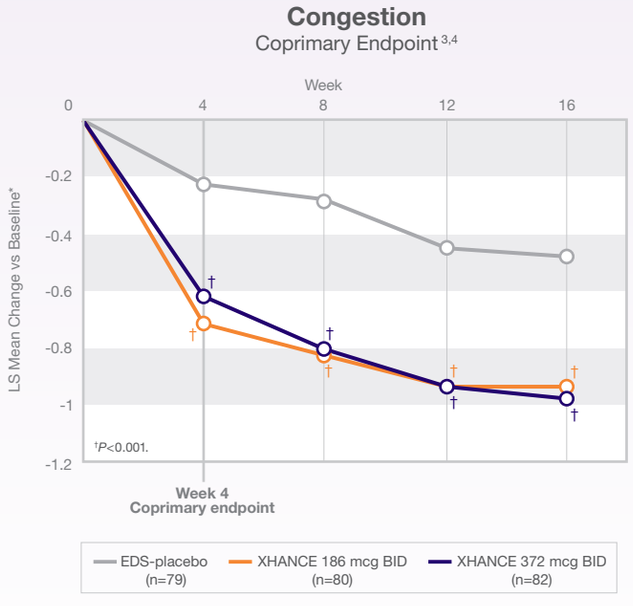
# Significant improvement in congestion

Results shown are from NAVIGATE II and are consistent with the results seen in NAVIGATE I




BID=twice daily.

*Least-squares mean change from baseline in patient-reported AM instantaneous diary scores for nasal symptoms on a scale from 0-3 (0=none, 1=mild, 2=moderate, 3=severe).

- Statistically significant onset of action was generally observed within 2 weeks[3]

### Study design summary

- NAVIGATE I and NAVIGATE II were double-blind, placebo-controlled trials lasting 16 weeks with an 8-week open-label extension evaluating patients with moderate-to-severe congestion and bilateral nasal polyps. All patients were dosed with XHANCE 372 mcg BID during the open-label extension.[3,4,9]

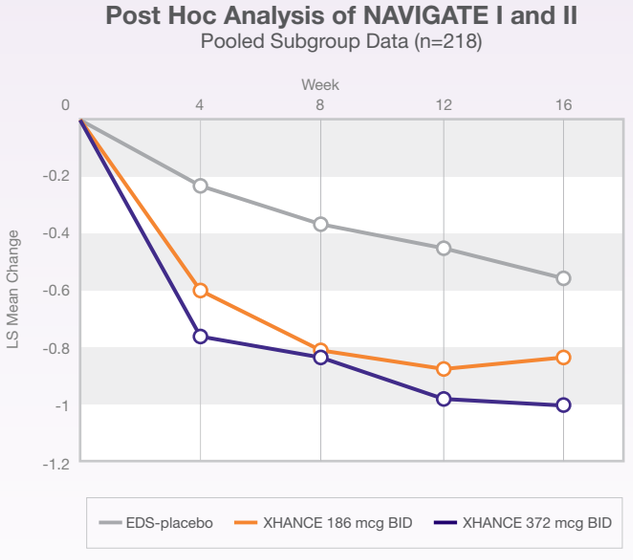
## IMPORTANT SAFETY INFORMATION

### WARNINGS AND PRECAUTIONS (continued):

- Hypercorticism and adrenal suppression may occur with very high dosages or at the regular dosage in susceptible individuals. If such changes occur, discontinue XHANCE slowly.



# Improvement in congestion in the subgroup of patients on a conventional nasal steroid spray at study entry[10]




- Subgroup of patients reporting use of a conventional nasal steroid spray within 30 days of the screening visit[10]
  - Patients reported a mean treatment duration of 3 years with a conventional nasal steroid spray
- **These results are descriptive and should be interpreted with caution**

## IMPORTANT SAFETY INFORMATION

### WARNINGS AND PRECAUTIONS (continued):

- Patients with major risk factors for decreased bone mineral content should be monitored and treated with established standards of care.

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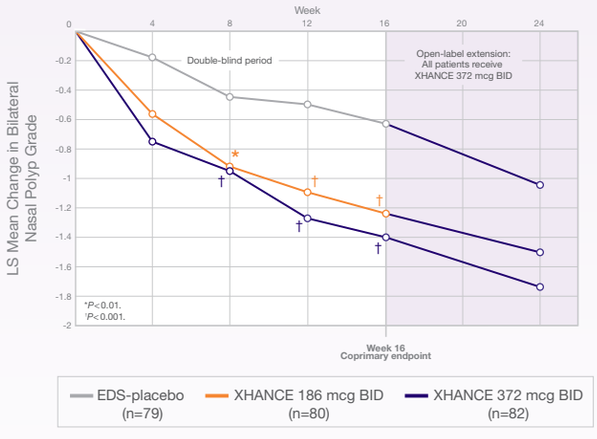
# Significant reduction in bilateral nasal polyp grade

Results shown are from NAVIGATE II and are consistent with the results seen in NAVIGATE I

**Bilateral Polyp Grade**
Coprimary Endpoint — Week 16[3,4]




Baseline grade: EDS-placebo, 3.8; XHANCE 186 mcg BID, 3.9; XHANCE 372 mcg BID, 3.9.

**In the XHANCE 372 mcg BID Treatment Group[4]:**

**69%** of patients experienced a ≥1-point reduction in bilateral polyp grade vs 40% with EDS-placebo at Week 16 (secondary endpoint)

**78%** of patients experienced a ≥1-point reduction in bilateral polyp grade at Week 24

**28%** of patients achieved polyp elimination (grade=0) in at least 1 nostril at Week 24

**Multiplicity adjustments were not applied for secondary endpoints; therefore, results could potentially represent chance findings. Furthermore, open-label results may be confounded by evaluator bias.**

## IMPORTANT SAFETY INFORMATION

### ADVERSE REACTIONS:

- The most common adverse reactions (incidence ≥ 3%) are epistaxis, nasal septal ulceration, nasopharyngitis, nasal mucosal erythema, nasal mucosal ulcerations, nasal congestion, acute sinusitis, nasal septal erythema, headache, and pharyngitis.



# Reduction in bilateral polyp grade in the subgroup of patients on a conventional nasal steroid spray at study entry[10]

**Post Hoc Analysis of NAVIGATE I and II**
Pooled Subgroup Data (n=218)


- Subgroup of patients reporting use of a conventional nasal steroid spray within 30 days of the screening visit[10]
  - Patients reported a mean treatment duration of 3 years with a conventional nasal steroid spray
- **These results are descriptive and should be interpreted with caution**

## IMPORTANT SAFETY INFORMATION

### DRUG INTERACTIONS:

- Strong cytochrome P450 3A4 inhibitors (e.g., ritonavir, ketoconazole): Use not recommended. May increase risk of systemic corticosteroid effects.

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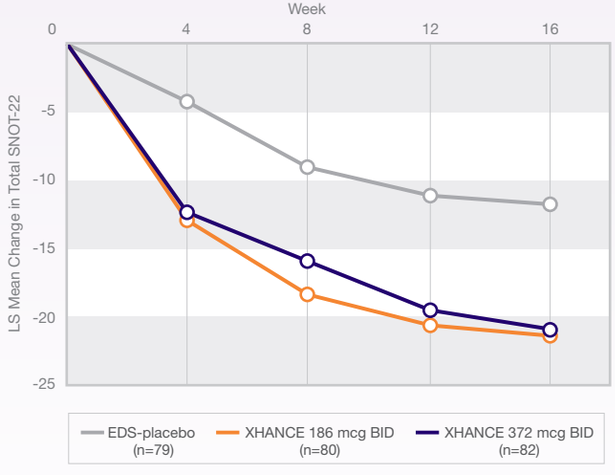
# Reduction in Sino-Nasal Outcome Test (SNOT-22) scores

## Results shown are from NAVIGATE II and are consistent with the results seen in NAVIGATE I

**SNOT-22[4,9*]**
Secondary Endpoint




*SNOT-22 is a questionnaire for assessing symptoms, quality of life, and functioning. Patients report answers to 22 questions using a scale from 0 ("no problem") to 5 ("problem as bad as can be"). Responses are summed, and total score ranges from 0 to 110, with a mean score of 9.3 for healthy patients.

**Multiplicity adjustments were not applied for secondary endpoints; therefore, results could potentially represent chance findings.**

- In medical literature, surgery has been reported to reduce SNOT-22 scores by 18 to 23 points from baseline[11,12]
- In a clinical trial, XHANCE reduced SNOT-22 scores by ~21 points from baseline at Week 16[4]
- In the clinical trials for XHANCE, the mean baseline SNOT-22 score for all arms was ~50[4,9]
- A change of ~9 points in SNOT-22 scores is considered the minimal clinically important difference[11,12]

**IMPORTANT SAFETY INFORMATION**

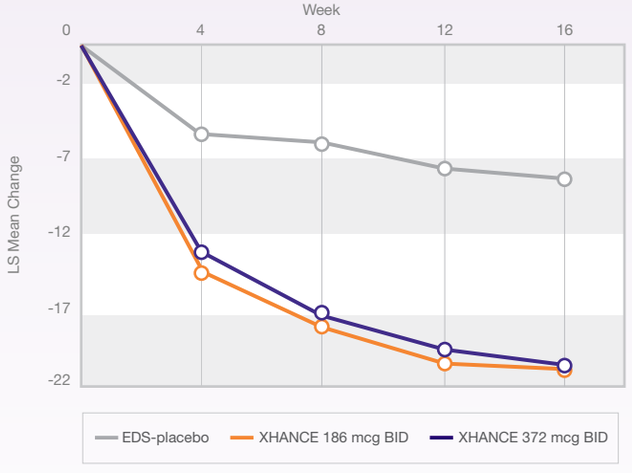
**USE IN SPECIFIC POPULATIONS:**

- Hepatic impairment. Monitor patients for signs of increased drug exposure.



# Reduction in SNOT-22 scores in the subgroup of patients on a conventional nasal steroid spray at study entry[10]

**Post Hoc Analysis of NAVIGATE I and II**
Pooled Subgroup Data (n=218)




- Subgroup of patients reporting use of a conventional nasal steroid spray within 30 days of the screening visit[10]
  - Patients reported a mean treatment duration of 3 years with a conventional nasal steroid spray
- **These results are descriptive and should be interpreted with caution**

**IMPORTANT SAFETY INFORMATION**

**WARNINGS AND PRECAUTIONS (continued):**

- Local Nasal Effects: epistaxis, erosion, ulceration, septal perforation, *Candida albicans* infection, and impaired wound healing. Monitor patients periodically for signs of possible changes on the nasal mucosa. Avoid use in patients with recent nasal ulcerations, nasal surgery, or nasal trauma.

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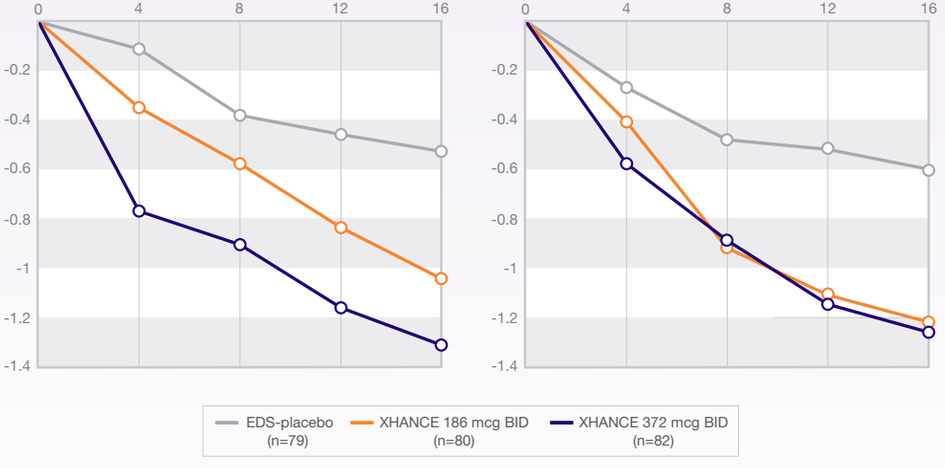
# Reduction in bilateral nasal polyp grade by subgroup of patients with or without sinus surgery

## Post Hoc Analysis of NAVIGATE I and II Pooled Data (N=481)

**Patients With Prior Sinus Surgery[13]**
(n=154)

**Patients Without Prior Sinus Surgery[13]**
(n=327)




- A post hoc analysis of a pooled population from NAVIGATE I and NAVIGATE II analyzed reduction in bilateral polyp grade in the subgroup of patients who had sinus surgery and those without sinus surgery prior to study entry[13]
- Patients were excluded from the studies if they had a history of sinus or nasal surgery within 6 months before screening[4,9]
- **The results shown above are descriptive and should be interpreted with caution**

**IMPORTANT SAFETY INFORMATION**

**WARNINGS AND PRECAUTIONS (continued):**

- Close monitoring for glaucoma and cataracts is warranted.
- Hypersensitivity reactions (e.g., anaphylaxis, angioedema, urticaria, contact dermatitis, rash, hypotension, and bronchospasm) have been reported after administration of fluticasone propionate. Discontinue XHANCE if such reactions occur.

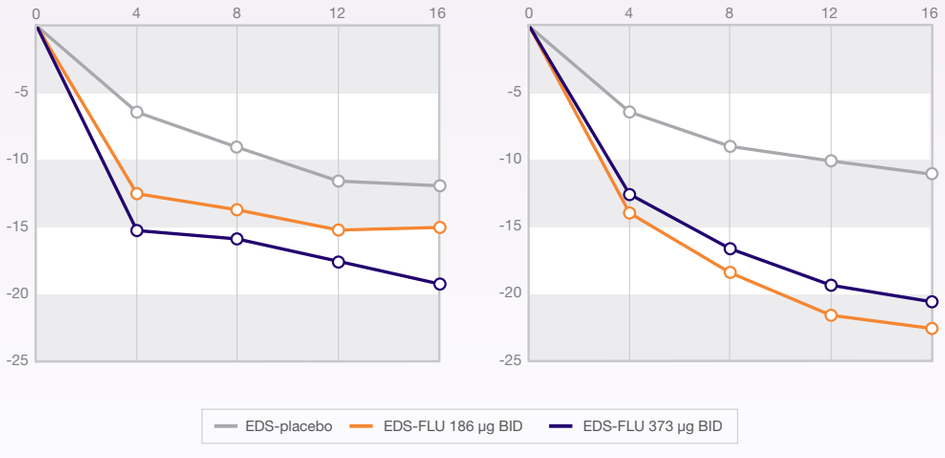


# Reduction in SNOT-22 score by subgroup of patients with or without sinus surgery

## Post Hoc Analysis of NAVIGATE I and II Pooled Data (N=481)

**Patients With Prior Sinus Surgery[13]**
(n=154)

**Patients Without Prior Sinus Surgery[13]**
(n=327)

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- **The results shown above are descriptive and should be interpreted with caution**

**IMPORTANT SAFETY INFORMATION**

**WARNINGS AND PRECAUTIONS (continued):**

- Immunosuppression: potential increased susceptibility to or worsening of infections (e.g., existing tuberculosis; fungal, bacterial, viral, or parasitic infection; ocular herpes simplex). Use with caution in patients with these infections. More serious or even fatal course of chickenpox or measles can occur in susceptible patients.

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# Well-characterized safety profile

## Summary of Adverse Reactions With XHANCE Reported in ≥3% of Subjects With Nasal Polyps and More Common Than Placebo in Placebo-Controlled Studies[3]

| Adverse Event (AE) | EDS-placebo BID (N=161) n (%) | XHANCE | |
|---|---|---|---|
| | | 186 mcg BID (N=160) n (%) | 372 mcg BID (N=161) n (%) |
| Epistaxis‡ | 4 (2.5) | 19 (11.9) | 16 (9.9) |
| Nasopharyngitis | 8 (5.0) | 3 (1.9) | 12 (7.5) |
| Nasal septal erosion and ulceration | 3 (1.9) | 11 (6.9) | 12 (7.5) |
| Nasal congestion | 6 (3.7) | 7 (4.4) | 9 (5.6) |
| Acute sinusitis | 6 (3.7) | 7 (4.4) | 8 (5.0) |
| Headache | 5 (3.1) | 8 (5.0) | 6 (3.7) |
| Pharyngitis | 2 (1.2) | 2 (1.3) | 5 (3.1) |
| Nasal mucosal erosion and ulceration | 2 (1.3) | 6 (3.8) | 4 (2.5) |
| Nasal mucosal erythema | 6 (3.7) | 9 (5.6) | 8 (5.0) |
| Nasal septal erythema | 3 (1.9) | 6 (3.8) | 7 (4.3) |

BID=twice daily.
‡Includes spontaneous adverse reaction reports.

The AEs observed during open-label trials of up to one year in subjects with chronic sinusitis with and without nasal polyps were similar to the AEs reported in placebo-controlled clinical trials in patients with nasal polyps.[4]



# IMPORTANT SAFETY INFORMATION

**CONTRAINDICATIONS:** Hypersensitivity to any ingredient in XHANCE.

**WARNINGS AND PRECAUTIONS:**

- Local Nasal Effects: epistaxis, erosion, ulceration, septal perforation, *Candida albicans* infection, and impaired wound healing. Monitor patients periodically for signs of possible changes on the nasal mucosa. Avoid use in patients with recent nasal ulcerations, nasal surgery, or nasal trauma.
- Close monitoring for glaucoma and cataracts is warranted.
- Hypersensitivity reactions (e.g., anaphylaxis, angioedema, urticaria, contact dermatitis, rash, hypotension, and bronchospasm) have been reported after administration of fluticasone propionate. Discontinue XHANCE if such reactions occur.
- Immunosuppression: potential increased susceptibility to or worsening of infections (e.g., existing tuberculosis; fungal, bacterial, viral, or parasitic infection; ocular herpes simplex). Use with caution in patients with these infections. More serious or even fatal course of chickenpox or measles can occur in susceptible patients.
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**DRUG INTERACTIONS:** Strong cytochrome P450 3A4 inhibitors (e.g., ritonavir, ketoconazole): Use not recommended. May increase risk of systemic corticosteroid effects.

**USE IN SPECIFIC POPULATIONS:** Hepatic impairment. Monitor patients for signs of increased drug exposure.

**References: 1.** American Rhinologic Society. Nasal Polyps. SINUSHEALTH website. https://sinushealth.com/conditions/treatment-of-nasal-polyps/. Accessed February 8, 2021. **2.** American Rhinologic Society and American College of Allergy, Asthma and Immunology. Treating Chronic Rhinosinusitis with Nasal Polyps Shared Decision-Making Tool. American College of Allergy, Asthma and Immunology. https://www.american-rhinologic.org/index.php?option=com_content&view=article&id=374:nosenews-sept-2020&catid=61:newsletter-archive#CRSwNPTool. Accessed March 22, 2021. **3.** Full Prescribing Information for XHANCE (fluticasone propionate). OptiNose US, Inc.; 2021. **4.** Leopold DA, Elkayam D, Messina JC, et al. NAVIGATE II: randomized double-blind trial of the exhalation delivery system with fluticasone (EDS-FLU) for nasal polyposis. *J Allergy Clin Immunol*. 2019;143(1):126-134. **5.** Djupesland PG. Nasal drug delivery devices: characteristics and performance in a clinical perspective—a review. *Drug Deliv Transl Res*. 2013;3(1):42-62. **6.** Leach CL, Kuehl PJ, Chand R, McDonald JD. Nasal deposition of HFA-beclomethasone, aqueous fluticasone propionate and aqueous mometasone furoate in allergic rhinitis patients. *J Aerosol Med Pulm Drug Deliv*. 2015;28(5):334-340. **7.** Siu J, Johnston JJ, Pontre B, Inthavong K, Douglas RG. Magnetic resonance imaging evaluation of the distribution of spray and irrigation devices within the sinonasal cavities. *Int Forum Allergy Rhinol*. 2019;9(9):958-970. **8.** Cho SH, Ledford D, Lockey RF. Medical management strategies in acute and chronic rhinosinusitis. *J Allergy Clin Immunol Pract*. 2020;8(5): 1559-1564. **9.** Sindwani R, Han JK, Soteres DF, et al. NAVIGATE I: randomized, placebo-controlled, double-blind trial of the Exhalation Delivery System with fluticasone for chronic rhinosinusitis with nasal polyps. *Am J Rhinol Allergy*. 2019;33(1):69-82. **10.** Senior BA, Schlosser RJ, Bosso J, Soler ZM. Efficacy of the exhalation delivery system with fluticasone in patients who remain symptomatic on standard nasal steroid sprays. *Int Forum Allerg Rhinol*. 2020. **11.** Hopkins C, Gillett S, Slack R, Lund VJ, Browne JP. Psychometric validity of the 22-item Sinonasal Outcome Test. *Clin Otolaryngol*. 2009;34(5):447-454. **12.** Le PT, Soler ZM, Jones R, et al. Systematic review and meta-analysis of SNOT-22 outcomes after surgery for chronic rhinosinusitis with nasal polyposis. *Otolaryngol Head Neck Surg*. 2018;159(3):414-423. **13.** Data on file. OptiNose US, Inc.

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