optinose®

Building a Leading ENT / Allergy Specialty Company

Needham Virtual Healthcare Conference

April 12, 2022

Forward-Looking Statements

This presentation and our accompanying remarks contain “forward-looking statements” within the meaning of the U.S. Private Securities Litigation Reform Act of 1995. All statements that are not historical facts are hereby identified as forward-looking statements for this purpose and include, among others, statements relating to: our growth strategy; potential for continued XHANCE prescription and net revenue growth and factors supporting such growth; prescription, refill and market share trends; potential effects of INS market seasonality on XHANCE prescriptions; potential early year effects on price and volume related to patient insurance; projected Company GAAP operating expenses and stock-based compensation for 2022; projected XHANCE net revenues for first quarter and full year 2022; projected XHANCE average net revenue per prescription for first quarter and full year 2022; the potential benefits of XHANCE for the treatment of chronic sinusitis; the expectation of having top-line results from ReOpen2 in the second quarter of 2022; the Company's plans to seek approval for a follow-on indication for XHANCE for the treatment of chronic sinusitis, the potential for XHANCE to be the first FDA-approved drug treatment for chronic sinusitis and the potential market expansion opportunities and other benefits of obtaining such indication; the Company's plan to secure a partnership to promote XHANCE in primary care and the prospects for, and potential benefits of, such potential partnership; and other statements regarding the Company’s future operations, financial performance, prospects, intentions, objectives and other future events.

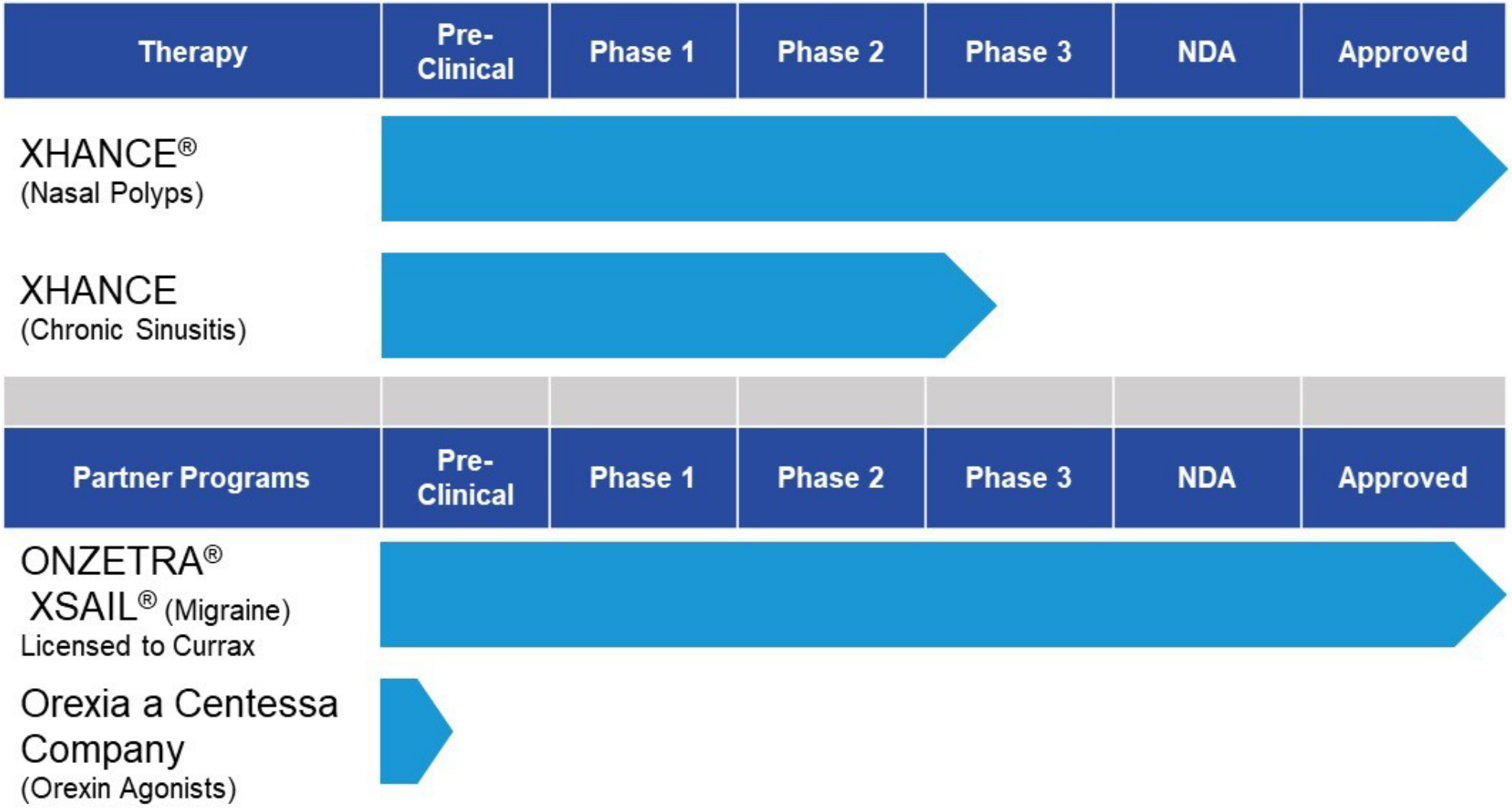
Forward-looking statements are based upon management’s current expectations and assumptions and are subject to a number of risks, uncertainties and other factors that could cause actual results and events to differ materially and adversely from those indicated by such forward-looking statements including, among others: impact of, and the uncertainties caused by, the COVID-19 pandemic; physician and patient acceptance of XHANCE for its current and any potential future indication; the Company’s ability to maintain adequate third party reimbursement for XHANCE (market access); the Company’s ability to grow XHANCE prescriptions and net revenues; the prevalence of chronic sinusitis and market opportunities for XHANCE may be smaller than expected; unexpected costs and expenses; potential for varying interpretation of the top-line results from ReOpen1 and the potential for the full data set, when available, to contain results that conflict with or are inconsistent with the top-line results; risks and uncertainties relating to the completion and results of ReOpen2; uncertainties related to the clinical development program and regulatory approval of XHANCE for the treatment of chronic sinusitis; the Company’s ability to comply with the covenants and other terms of the Pharmakon note purchase agreement; risks and uncertainties relating to intellectual property; and the risks, uncertainties and other factors discussed in the “Risk Factors” section and elsewhere in our most recent Form 10-K and Form 10-Q filings with the Securities and Exchange Commission – which are available at http://www.sec.gov. As a result, you are cautioned not to place undue reliance on any forward-looking statements. Any forward-looking statements made in this presentation speak only as of the date of this presentation, and we undertake no obligation to update such forward-looking statements, whether as a result of new information, future developments or otherwise.

Our Growth Strategy

- Continue commercial growth of XHANCE in the ENT and allergy specialty segments in the U.S.
- Complete R&D program seeking XHANCE indication as first-in-class treatment of chronic sinusitis to expand specialty opportunity and enable extension by partnership into primary care
- Create leverage with our current footprint in ENT and allergy specialty space by seeking complementary approved or development products or partnerships
- Explore additional business development activities for EDS technology outside of the ENT and allergy segments
- Remain opportunistic in pursuit of select opportunities to expand XHANCE into international markets

optinose

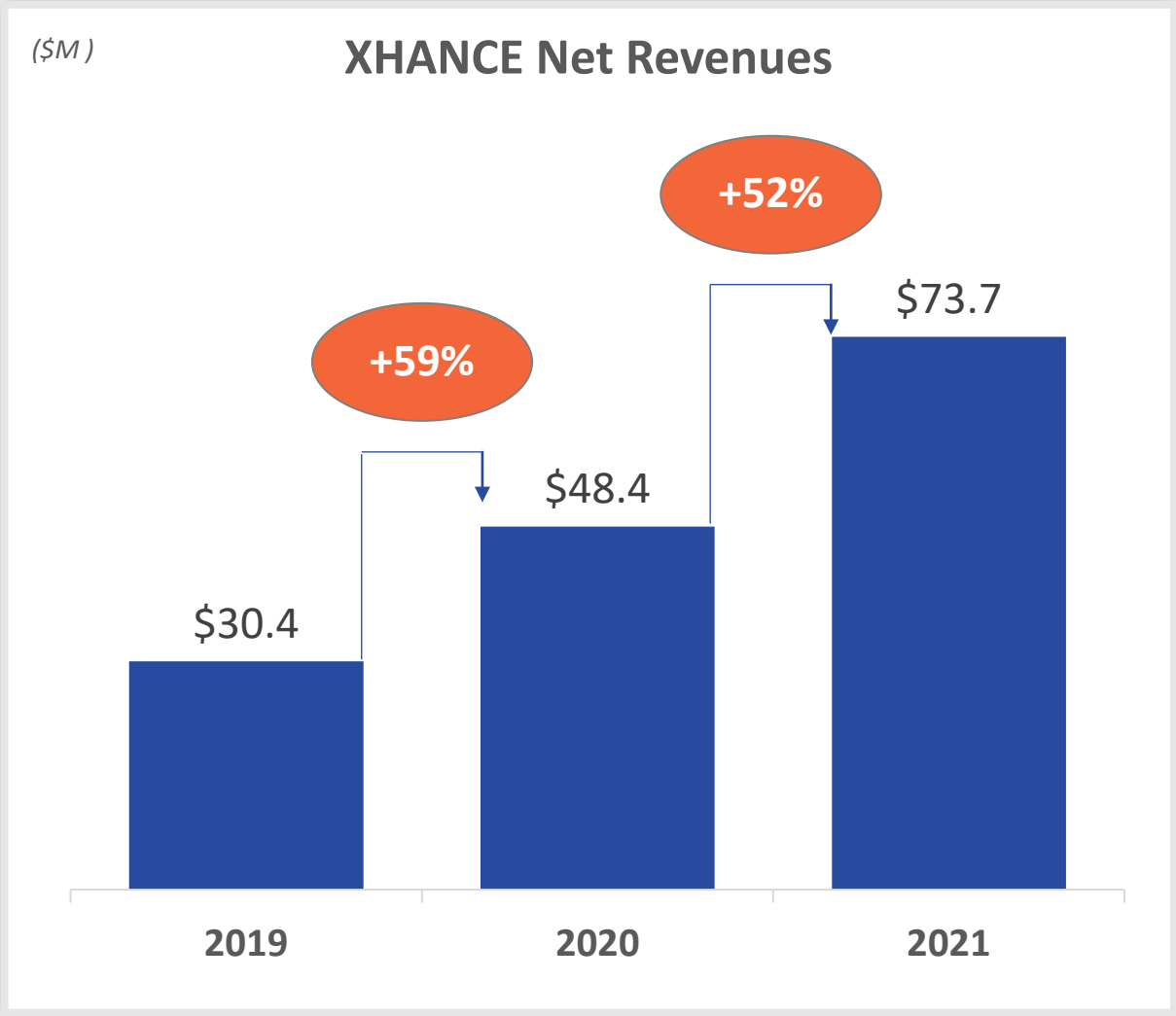
Our Pipeline



optinose®

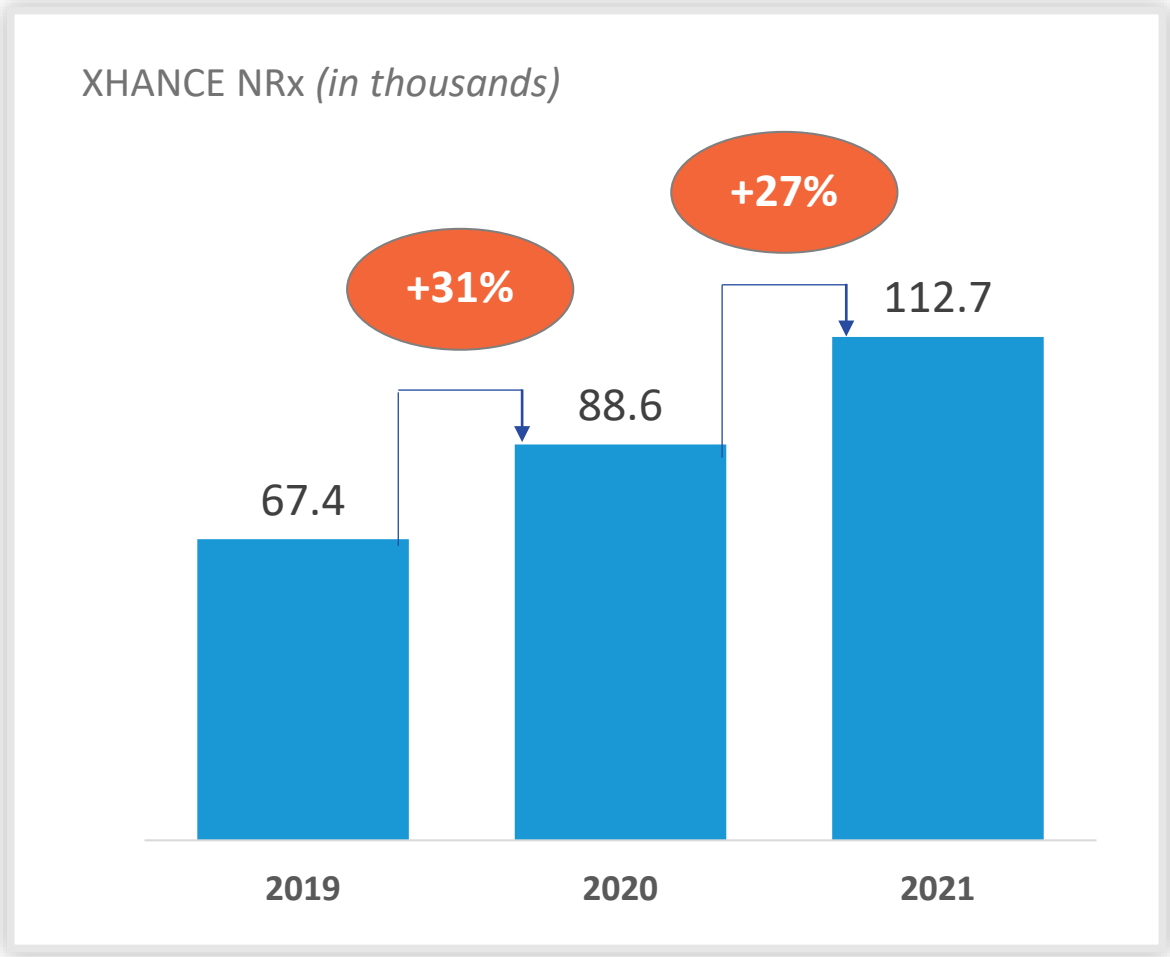
Commercializing XHANCE® (fluticasone propionate) as Treatment for Nasal Polyps

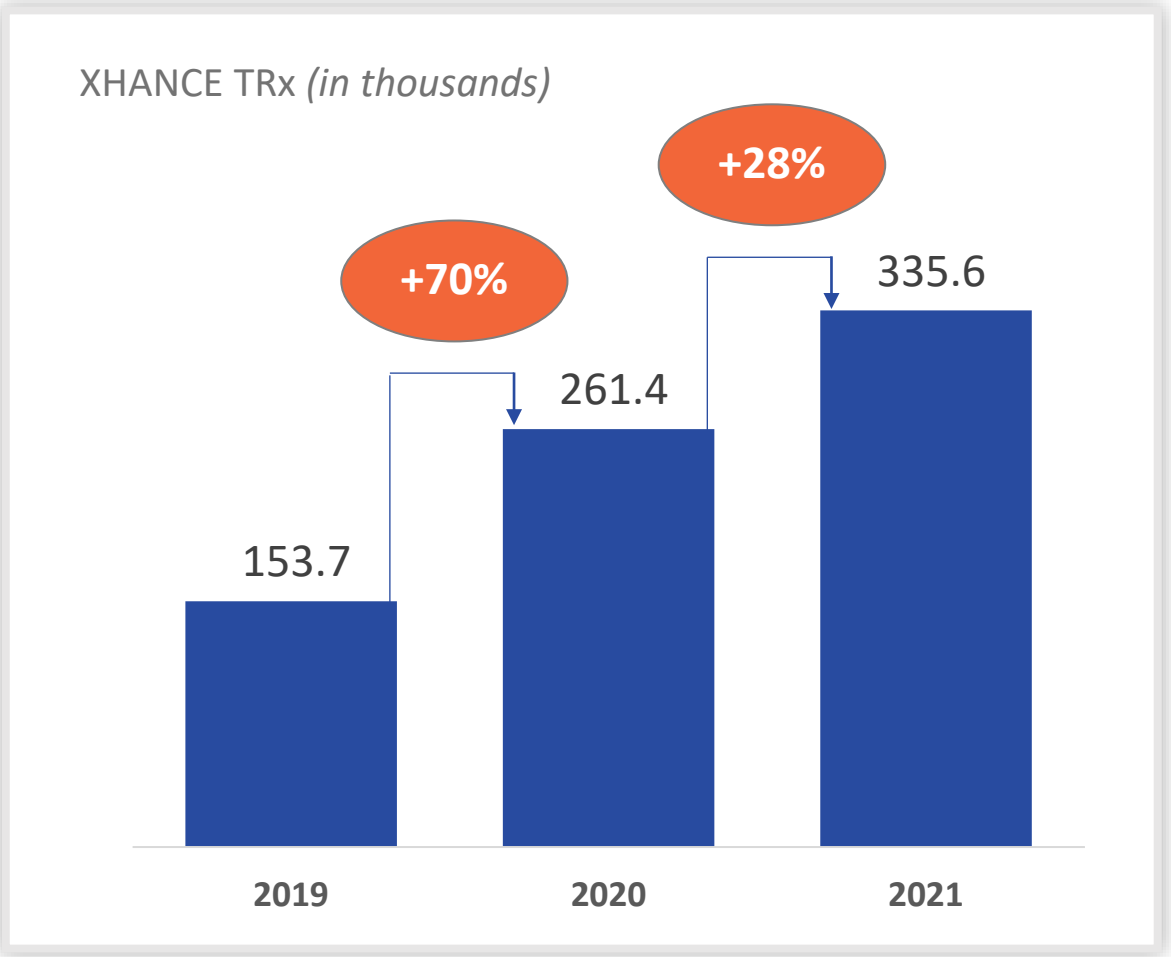
We Delivered Annual XHANCE Net Revenue Increases of More Than 50% in 2020 and 2021 With Our Commercial Model



- We have a sales force covering ~100 territories who target over 10,000 ENT and allergy specialists and "specialty-like" primary care physicians
- In addition, we target physicians through digital and non-personal promotion to create a total target audience of approximately 18,000 physicians
- Eligible commercially insured patients may obtain XHANCE for as little as $0 out-of-pocket through the XHANCE co-pay assistance program
- Approximately 80% of commercially insured lives are currently in a plan that covers XHANCE

We Delivered Strong New and Total Prescription Growth in 2020 and 2021 During a Challenging Period for the INS Market





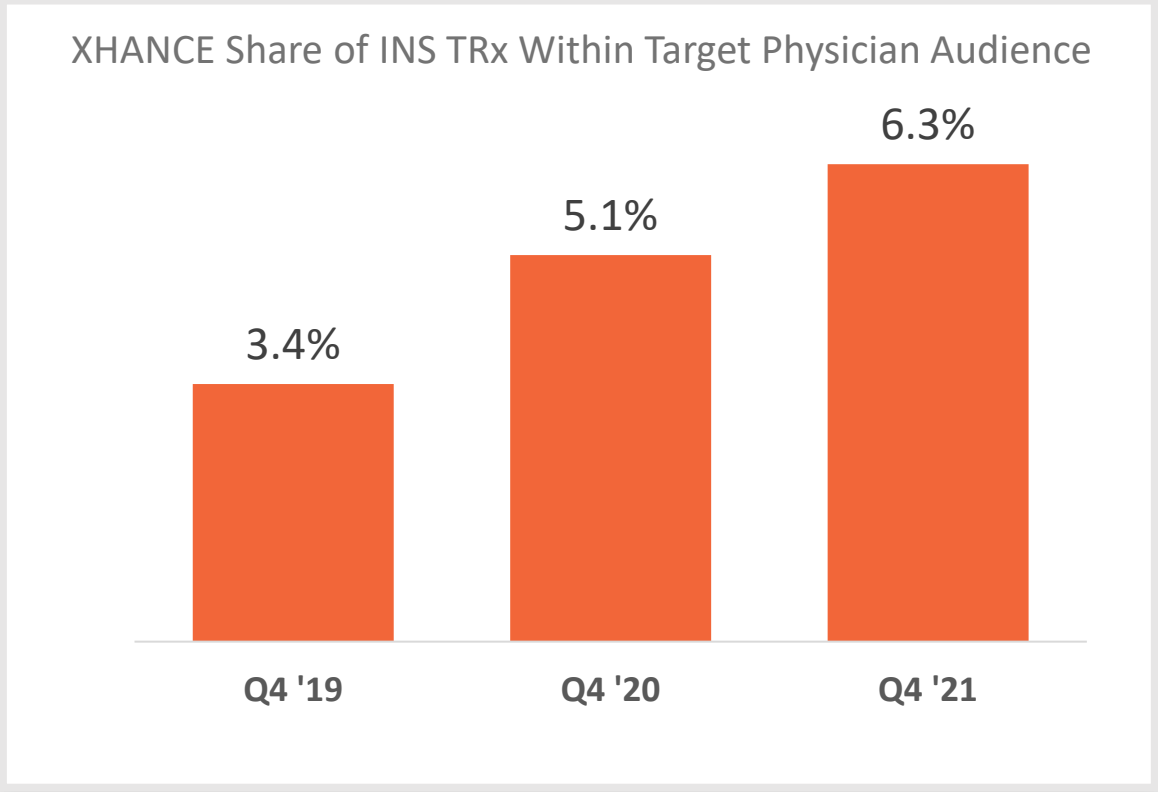
NRx for Intranasal Steroids Market decreased 13% from 2019 to 2020 and increased 4% from 2020 to 2021
TRx for Intranasal Steroids Market decreased 7% from 2019 to 2020 and increased 0% from 2020 to 2021

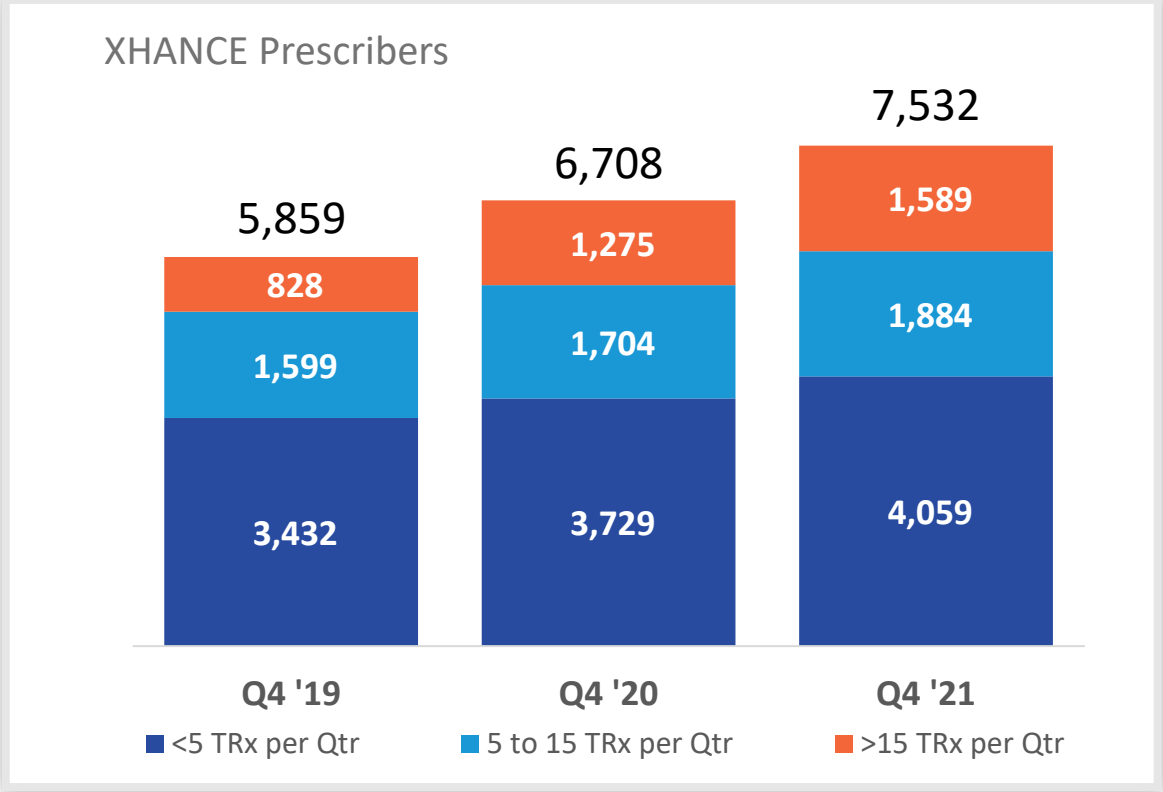
Estimated based on monthly prescription data from third parties and XHANCE preferred pharmacy network. The Market on this slide is defined as the sum of all intranasal steroid prescriptions based on monthly prescription data from third parties

optinose®

Growing XHANCE Market Share and Number of Frequent Prescribers

XHANCE market share increased from 3.4% to 6.3% From Q4 2019 to Q4 2021 and HCPs who had more than 15 XHANCE prescriptions increased by 92% (828 to 1,589) from Q4 2019 to Q4 2021

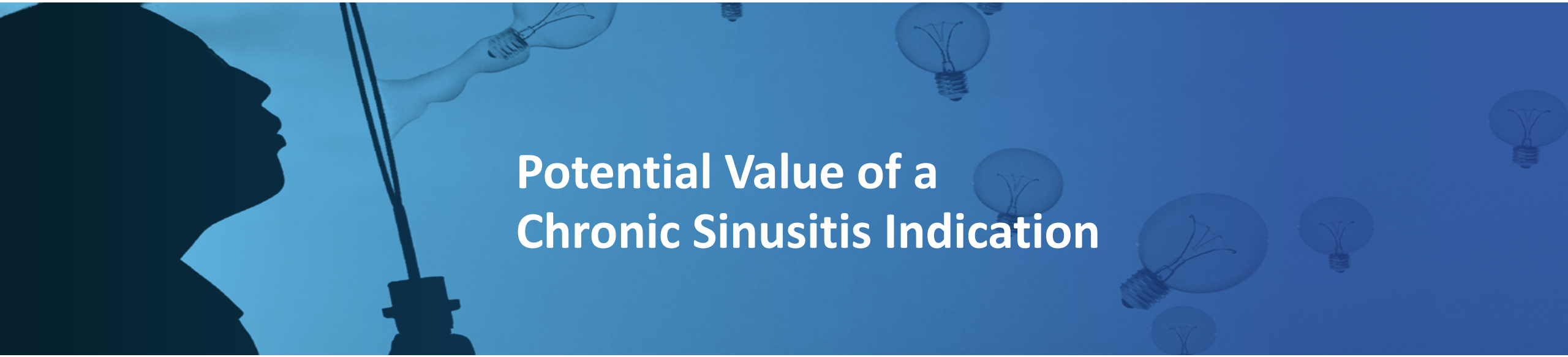




The Market on this slide is defined as the sum of all intranasal steroid prescriptions written by physicians in the XHANCE target physician audience of approximately 18,000 physicians.
Estimated based on monthly prescription data from third parties and XHANCE preferred pharmacy network.

optinose®

optinose®



Potential Value of a Chronic Sinusitis Indication

What is Chronic Sinusitis (CS)

CS is an inflammatory disease of the paranasal sinuses that is defined by the presence of at least two out of four cardinal symptoms (i.e., facial pain/pressure, hyposmia/anosmia, nasal drainage, and nasal obstruction) for at least 12 consecutive weeks, in addition to objective evidence of sinus disease

Prevalence

- Up to **30 Million** US Adults suffer from symptoms of CS and there are no FDA-approved drug treatments
- Approximately **10 Million** patients are currently treated by a physician annually

High Burden

- Disease persists for many years
- Significant harm to quality of life, comparable in magnitude to CHF or COPD

Sources: Sedaghat AR. Chronic Rhinosinusitis. Am Fam Physician. 2017 Oct 15;96(8):500-506. PMID: 29094889. Palmer J et al . A cross-sectional population-based survey of the prevalence, disease burden, and characteristics of the US adult population with symptoms of chronic rhinosinusitis (CRS). Poster session presented at: 62nd Annual Meeting of the American Rhinologic Society; September 16-17, 2016; San Diego, CA. Optinose Market Research. Data on file.

optinose®

Successful Development of XHANCE as the First FDA-approved Drug Treatment for Chronic Sinusitis Creates Multiple New Opportunities for Growth

Today

1 Million

optinose®

Up to approximately **1 Million** patients with diagnosed nasal polyps (NP) are treated by specialty physicians who are the current focus of our sales deployment

With a CS Indication

3 million

optinose®

Up to approximately **3 Million** patients with either NP or CS are treated by specialty physicians who are the focus of our current sales deployment

10 Million

Up to approximately **10 Million total** patients with NP or CS are treated by a physician annually

For a Partner, there are **6 to 7 million** NP+CS patients currently treated by a Primary Care Physician and **20 million** lapsed patients that could be activated

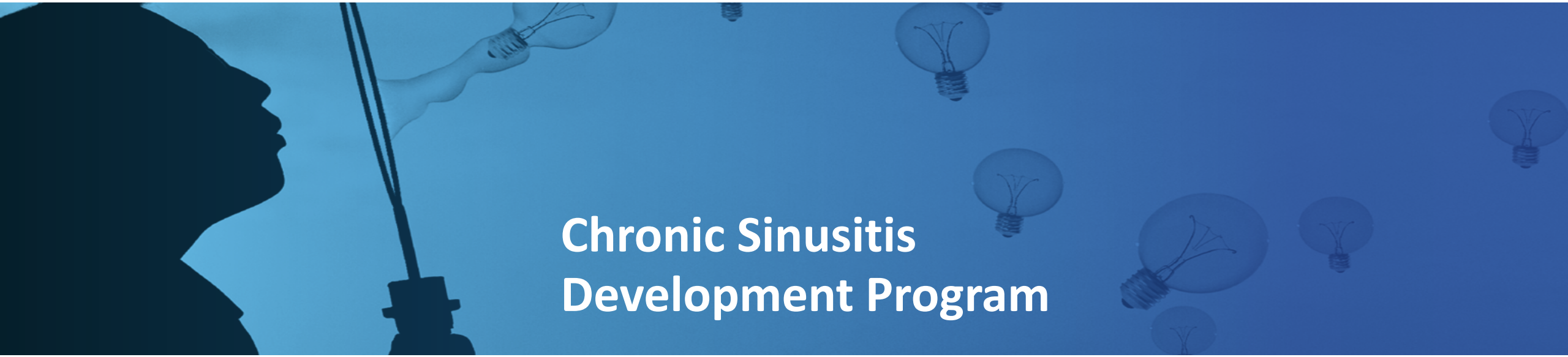
optinose®

Successful Development of XHANCE as a Treatment for Chronic Sinusitis Would Increase Opportunity and Address Certain Barriers to Broader Prescribing that Exist Today

Insurance

- Today, **~80%** of commercial lives are in plans that cover XHANCE, but **~half** require physicians to attest that they are prescribing for the approved indication
- This is important because chronic sinusitis (CS) is diagnosed much more frequently than nasal polyps (NP)
- **~10 million** patients diagnosed with CS/NP are actively treated by physicians compared to **~1 million** with NP

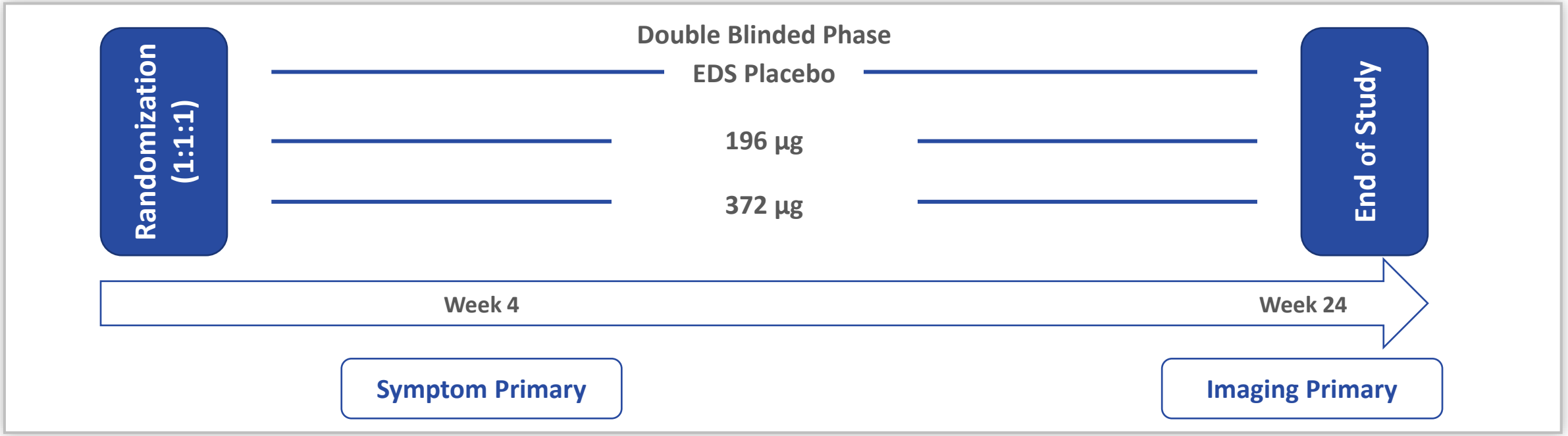
optinose®



Chronic Sinusitis Development Program

ReOpen1 and ReOpen2 Trial Design Summary

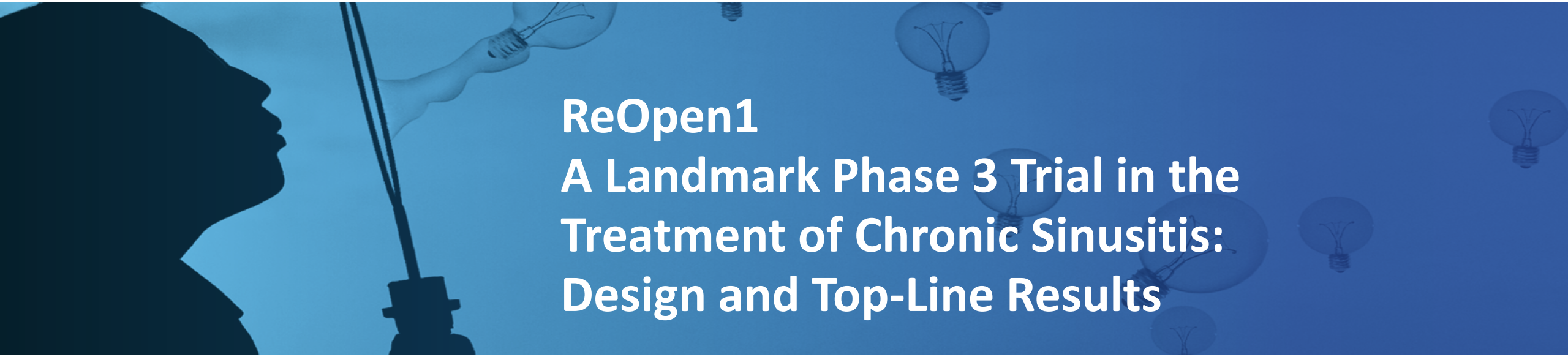
Randomized, double-blind, EDS-placebo-controlled, parallel-group, multicenter studies to evaluate efficacy and safety of XHANCE 186 µg (1 spray) and 372 µg (2 sprays) BID in subjects with CS



ReOpen1 Enrolled 332 patients with CS of which 205 Evaluable Subjects also had Nasal Polyps
ReOpen2 Enrolled ~210 patients with CS and no concomittant Nasal Polyps

optinose®

optinose®



ReOpen1
A Landmark Phase 3 Trial in the Treatment of Chronic Sinusitis: Design and Top-Line Results

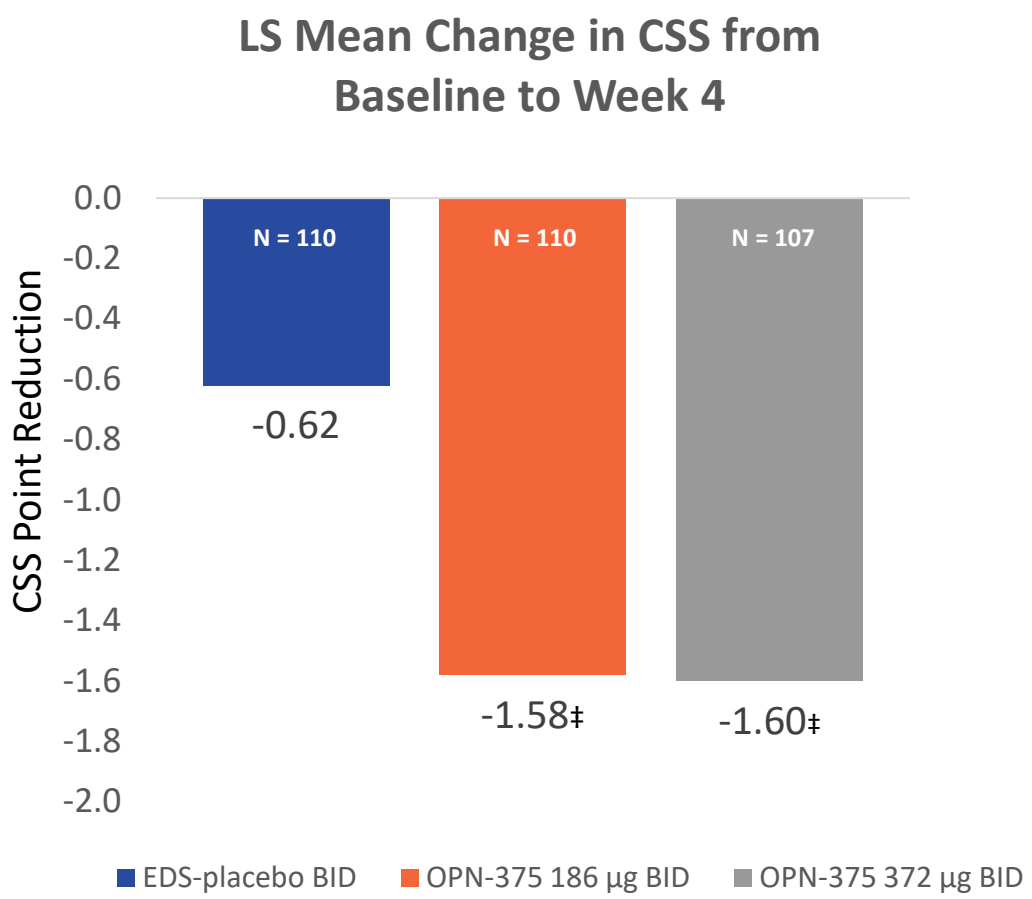
Re-Open 1: Disposition and Baseline Characteristics

	EDS Placebo	XHANCE 186 mcg	XHANCE 372 mcg
Subjects Randomized	112	111	109
Subjects Who Completed Study	96	102	101
Subjects Discontinuing Early*	16	9	8
Full Analysis Set	110	110	107
Evaluable subjects with NP	69	69	67
Evaluable subjects without NP	41	41	40
Mean Baseline CSS Score (Symptom scoring)	5.77	5.42	5.48
Mean Baseline APOV (CT scan scoring)	68.94	68.88	68.95
Mean Baseline SNOT-22 Score	48.0	50.94	50.81

APOV (average percent of opacified volume); **CSS** (composite symptom score); **SNOT-22** (Sino-Nasal Outcome Test, 22 item)

* Lack of efficacy was the most common reason for early discontinuation

ReOpen-1: Combined Symptom Score Coprimary Endpoint



BID, twice daily; CSNS, composite symptom nasal score.

‡*P* ≤ .001 vs EDS-placebo

Summary

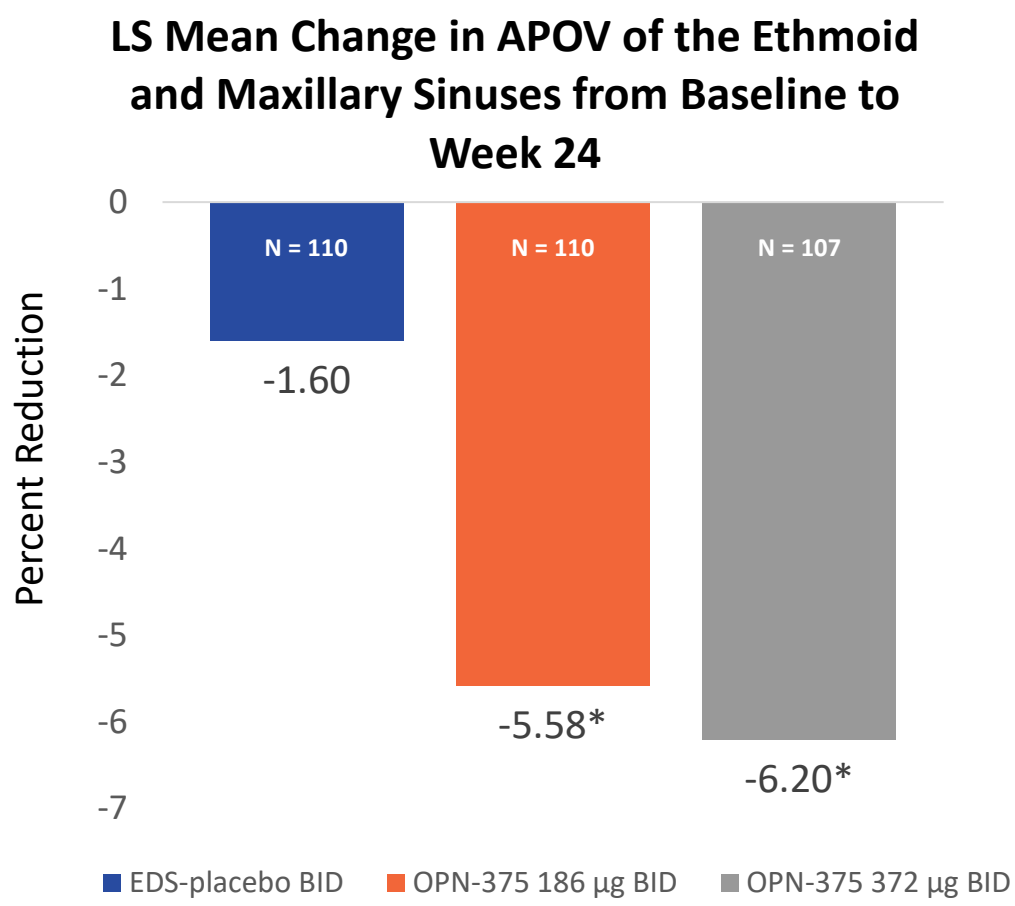
- Magnitude of symptom improvement comparable to NAVIGATE I and II
- Treatment with XHANCE improved CSS and each of the four cardinal symptoms at week 4

ReOpen-1: Average Percent Opacified Volume (Ethmoid and Maxillary)

Objective CT scan Coprimary Endpoint

Summary

- First phase 3 trial to demonstrate statistically significant improvement in sinus opacification with a nasal treatment
- Represents an average ~20% increase in sinus patency for patients treated with XHANCE



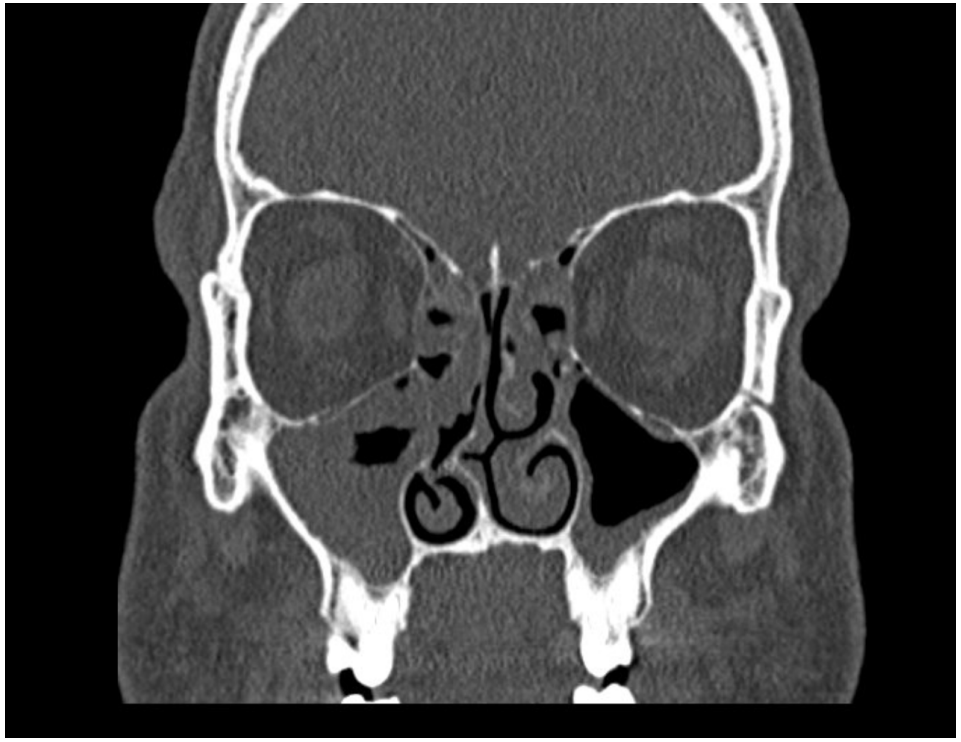
APOV, average percent of opacified volume; BID, twice daily;.

*$P \leq .05$ vs EDS placebo.

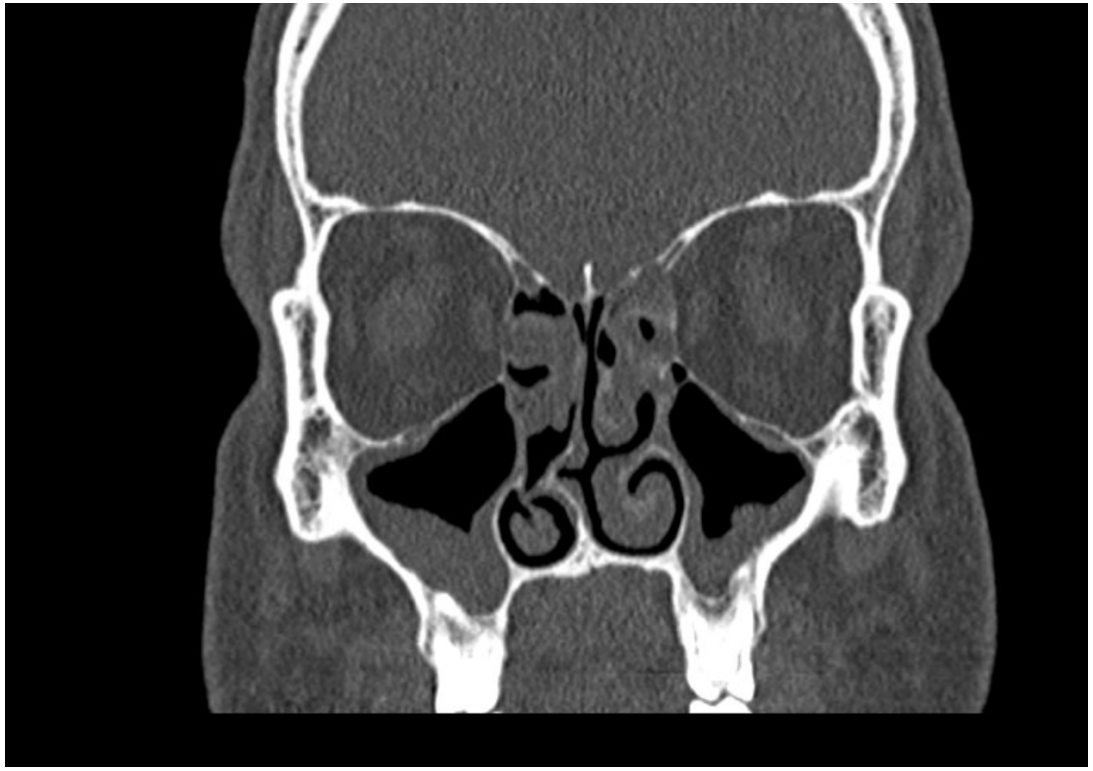
optinose®

Illustration of APOV Improvement (Patient Receiving XHANCE 186 µg BID)

Baseline



Week 24



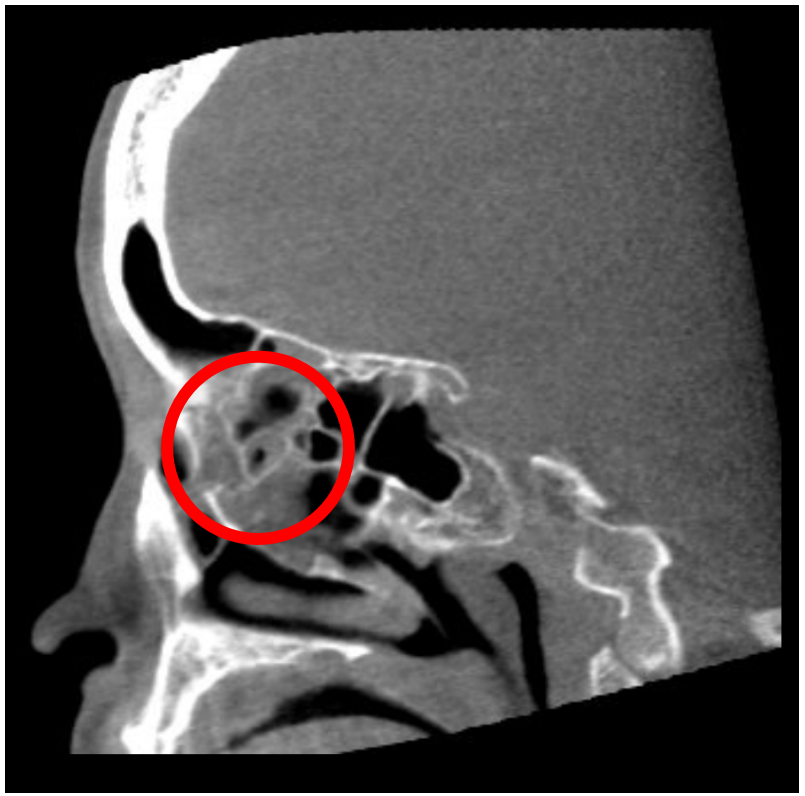
6.4% Improvement on APOV

Images reflect individual results and results and may not be representative of results generally.

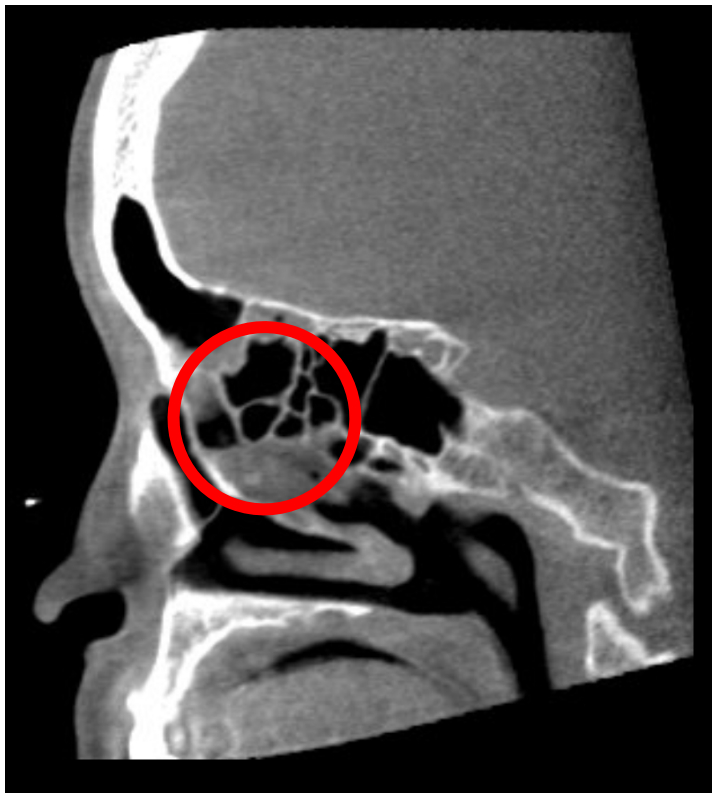
optinose®

Illustration of APOV Improvement (Patient Receiving XHANCE 372 µg BID)

Baseline



Week 24



7.0% Improvement on APOV

Images reflect individual results and results and may not be representative of results generally.

optinose®

Secondary Endpoints and Subgroup Analysis

Top-line results: full analyses to follow

Secondary Endpoints

Exploratory and Subject to Nominal Statistical Testing

- **Four defining symptoms of Chronic Sinusitis -** XHANCE-treated patients had statistically significant improvement over EDS-placebo treated patients on each of the four symptoms (congestion, rhinorrhea, facial pain/pressure, and sense of smell) at week 4
- **Acute Exacerbations -** XHANCE-treated patients had a reduced occurrence of acute disease exacerbation which reached statistical significance in the high dose group
- **SNOT-22 -** XHANCE-treated patients had statistically significant improved SNOT-22 scored by week 4 compared to EDS-placebo treated patients

Subgroup Analyses

Exploratory and Nominal Statistical Testing
Underpowered to Detect Statistically Significant Differences

- **CSS Outcome –** the subgroup of chronic sinusitis patients without concomitant nasal polyps and the subgroup with concomitant nasal polyps who received XHANCE both had statistically significant improvement in CSS over EDS-placebo treated patients
- **APOV Outcome –** the subgroup of chronic sinusitis patients without concomitant nasal polyps receiving XHANCE was not statistically different from those receiving EDS-placebo and the subgroup with concomitant nasal polyps receiving XHANCE was statistically significantly improved over EDS-placebo patients

AEs Occurring in ≥3% of Patients and More Common Than Placebo

Adverse Event (AE)	EDS-placebo BID (N =112) n (%)	XHANCE 186 mcg BID (N =111) n (%)	XHANCE 372 mcg BID (N =109) n (%)
Epistaxis	1 (0.9)	5 (4.5)	13 (11.9)
Nasopharyngitis	3 (2.7)	6 (5.4)	3 (2.8)
Asthma	1 (0.9)	5 (4.5)	4 (3.7)
Nuclear Cataract	0	5 (4.5)	4 (3.7)
Cortical Cataract	1 (0.9)	6 (5.4)	2 (1.8)
Subcapsular Cataract	2 (1.8)	1 (0.9)	1 (0.9)

Additional Phase 3b Clinical Trial Data Expected in Q2 2022

ReOpen·1 study

Recruitment Completed July 2021

Top-line results presented in Q1 2022 ✓

ReOpen·2 study

Recruitment Completed October 2021

Top-line results expected in Q2 2022

ReOpen1 ClinicalTrials.gov Identifier: NCT03781804 Enrolled 332 patients with CS of which 205 Evaluable Subjects had Nasal Polyps
ReOpen2 ClinicalTrials.gov Identifier: NCT03781804 Enrolled ~210 patients with CS without Nasal Polyps

optinose®

Additional Financial Information

XHANCE Gross Margin Percentage and Consistent R&D plus SG&A Expense Have Enabled Revenue Growth to Translate to Decreasing Operating Loss

($000s)	2019	2020	2021
XHANCE Net Revenue	30,401	48,357	73,652
Licensing Revenues	4,230	750	1,000
Total Revenues	34,631	49,117	74,652
Cost of Product Sales	5,294	7,520	9,151
Gross Margin % [1]	*86.1%*	*84.4%*	*87.6%*
Research and Development	20,783	23,378	25,318
Selling, General and Administrative	104,155	105,438	106,633
Total SG&A + R&D	124,938	128,816	131,951
Loss from Operations	(95,601)	(87,219)	(66,450)

The Chronic Sinusitis Development Program Drove ~$23 Million of R&D Expenses in 2021 (trials end in 2022)

1 Gross margin % as shown is calculated as (XHANCE Net Revenues – Cost of Product Sales)/(XHANCE Net Revenues)

optinose®

Full Year 2022 Financial Guidance

- **XHANCE Net Revenue**
  - Expected to be at least $90 million
- **XHANCE Average Net Revenue per Prescription**
  - FY 2022 expected to exceed $210
- **Operating Expense (GAAP)**
  - Expected to be between $135 – $140 million; approximately $10 million of which represents stock-based compensation

Investor Relations – NASDAQ: OPTN

At 31 December 2021:

- **$111 million** in cash
- Long-term debt: **$130 million**
- **82.2 million** common shares o/s
- **12.4 million** options, warrants & RSUs o/s

Optinose Investor Contact

Jonathan Neely,
VP, Investor Relations and Business Development
267-521-0531
Investors@optinose.com

 investors@optinose.com

 www.optinose.com

 @optinose

1 - Optinose is followed by the analysts listed above. Please note that any opinions, estimates or forecasts regarding the Company's performance made by these analysts are theirs alone and do not represent opinions, forecasts or predictions of Optinose or its management. Optinose does not by its reference above or distribution imply its endorsement of or concurrence with such information, conclusions or recommendations.

optinose®

Building a Leading ENT / Allergy Specialty Company

Needham Virtual Healthcare Conference

April 12, 2022