VANDA PHARMACEUTICALS INC.

2023 CORPORATE PRESENTATION

November 2023

Forward-Looking Statements

Various statements in this presentation, including, but not limited to statements regarding Vanda's commercial products, plans and opportunities, as well as statements about Vanda's products in development and the related clinical development and regulatory timelines and commercial potential for such products, are "forward-looking statements" under the securities laws. All statements other than statements of historical fact are statements that could be deemed forward-looking statements. Forward-looking statements are based upon current expectations and assumptions that involve risks, changes in circumstances and uncertainties. If the risks, changes in circumstances or uncertainties materialize or the assumptions prove incorrect, Vanda's results may differ materially from those expressed or implied by such forward-looking statements. Therefore, no assurance can be given that the results or developments anticipated by Vanda will be realized or, even if substantially realized, that they will have the expected consequences to, or effect on, Vanda. Important factors that could cause actual results to differ materially from those reflected in Vanda's forward-looking statements include, among others: Vanda's ability to continue to commercialize HETLIOZ® for the treatment of Non-24-Hour Sleep-Wake Disorder (Non-24) in the U.S., in light of existing and potential generic competition, and Europe and for the treatment of nighttime sleep disturbances in Smith-Magenis Syndrome (SMS) in the U.S.; Vanda's ability to increase market awareness of Non-24 and SMS and market acceptance of HETLIOZ®; Vanda's ability to obtain regulatory approval in Europe for HETLIOZ® in SMS; Vanda's ability to overcome the increased reimbursement challenges it faces as a result of declining third-party payor coverage; Vanda's ability to continue to generate U.S. sales of Fanapt® for the treatment of schizophrenia; Vanda's ability to complete the clinical development of and obtain regulatory approval of tradipitant in the treatment of gastroparesis, motion sickness and atopic dermatitis, HETLIOZ® in the treatment of jet lag disorder, insomnia, delayed sleep phase disorder and pediatric Non-24, Fanapt® in the treatment of bipolar I disorder in adults, the Fanapt® long acting injectable, VTR-297 in the treatment of hematologic malignancies, VSJ-110 for the treatment of dry eye, VPO-227 for the treatment of secretory diarrhea disorders, including cholera, VQW-765 for the treatment of social/performance anxiety, and VHX-896 for the treatment of psychiatric disorders; Vanda's ability to progress VCA-894A in Charcot-Marie-Tooth Disease, Type 2S; Vanda's dependence on third-party manufacturers to manufacture HETLIOZ® and Fanapt® in sufficient quantities and quality; Vanda's ability to prepare, file, prosecute, defend and enforce any patent claims and other intellectual property rights; Vanda's ability to maintain rights to develop and commercialize Vanda's products under its license agreements; Vanda's ability to obtain and maintain regulatory approval of Vanda's products, and the labeling for any approved products; Vanda's level of success in commercializing HETLIOZ® and Fanapt® in new markets; Vanda's expectations regarding the timing and success of preclinical studies and clinical trials; the safety and efficacy of Vanda's products; regulatory developments in the U.S., Europe and other jurisdictions; limitations on Vanda's ability to utilize some or all of its prior net operating losses and orphan drug and research development credits; the size and growth of the potential markets for Vanda's products and the ability to serve those markets; Vanda's expectations regarding trends with respect to its revenues, costs, expenses, liabilities and cash, cash equivalents and marketable securities; Vanda's ability to identify or obtain rights to new products; Vanda's ability to attract and retain key scientific or management personnel; the costs and effects of litigation; Vanda's ability to obtain the capital necessary to fund its research and development or commercial activities; the costs and effects of litigation; potential losses incurred from product liability claims made against Vanda; the use of existing cash, cash equivalents and marketable securities and other factors that are described in the "Cautionary Note Regarding Forward-Looking Statements", "Risk Factors" and "Management's Discussion and Analysis of Financial Condition and Results of Operations" sections of Vanda's most recent annual report on Form 10-K, as updated by Vanda's subsequent quarterly reports on Form 10-Q, current reports on Form 8-K and other filings with the SEC, which are available on the SEC's website at www.sec.gov.

Vanda cautions investors not to rely too heavily on the forward-looking statements contained in this presentation. The information in this presentation is provided only as of the date of this presentation, and Vanda undertakes no obligation, and specifically declines any obligation, to update or revise publicly any forward-looking statements, whether as a result of new information, future events, or otherwise, except as required by law.

Vanda Pharmaceuticals Inc. (VNDA)

Vanda is a leading global biopharmaceutical company dedicated to innovating in the service of people's pursuit of happiness

Commercialized Products

HETLIOZ®
HETLIOZ LQ®

Fanapt®

Robust pipeline

Recent regulatory submissions

Multiple products across wide range of therapeutic areas

Strong Financial Position

Approx. $490 million cash as of Q3 2023 with no debt

Commercialized Products

- HETLIOZ® oral capsules are approved in the U.S. and Europe for the treatment of Non-24-Hour Sleep-Wake Disorder (Non-24).
- HETLIOZ® oral capsules and HETLIOZ LQ® liquid formulation are approved in the U.S. for the treatment of nighttime sleep disturbances in adults and children, respectively, with Smith-Magenis Syndrome (SMS).
- Pursuing FDA approvals for HETLIOZ® in the indications of insomnia and jet lag disorder.

- Fanapt® is approved in the U.S. for the treatment of adults with schizophrenia.
- Positive results in the Phase III clinical study of Fanapt® in acute manic and mixed episodes associated with bipolar I disorder in adults. Pursuing FDA approval for Fanapt® in the indication of bipolar I disorder in adults.

Clinical Development Pipeline

Product	Indication	Preclinical	Phase I	Phase II	Phase III	Regulatory
Hetlioz® (tasimelteon) capsules 20 mg	Jet Lag Disorder					
	Insomnia					
	Delayed Sleep Phase Disorder (DSPD)					
	Non-24 Pediatric					
Fanapt® (iloperidone) tablets 1 mg, 2 mg, 4 mg, 6 mg, 8 mg, 10 mg, 12 mg	Bipolar I Disorder					
	Long Acting Injectable (LAI)					
VHX-896	Schizophrenia					
	Bipolar I Disorder					
Tradipitant	Gastroparesis					
	Motion Sickness					
	Atopic Dermatitis					
VTR-297	Hematologic Malignancies					
CFTR	VSJ-110 (Activator)					
	VPO-227 (Inhibitor)					
VQW-765	Social/Performance Anxiety					

Clinical Development Pipeline: Key Milestones

Vanda pursuing FDA approval for the following:

Product	Indication
Fanapt®	Bipolar (PDUFA Date: 4/2/2024)
HETLIOZ®	Insomnia (PDUFA Date: 3/4/2024)
Tradipitant	Gastroparesis (Approx. Mid-2024)

Other recent clinical and regulatory developments include:

Indication	Recent Action
Motion sickness	Positive Phase III results; second Phase III study initiated
Charcot-Marie-Tooth Disease, Type 2S	Orphan drug designation granted for VCA-894A
Cholera	Orphan drug designation granted for VPO-227

2022 Financial Performance

Full Year 2022 Revenue

$254.4 million

HETLIOZ® net product sales were $159.7 million for the full year 2022

Fanapt® net product sales were $94.7 million for the full year 2022

Cash as of December 31, 2022

$466.9 million

Cash as of September 30, 2023 was $489.9 million

2023 Financial Highlights

Q3 2023 Financial Highlights

$38.8 million

Total net product sales from HETLIOZ® and Fanapt® were $38.8 million in the third quarter of 2023

Hetlioz® (tasimelteon) capsules 20 mg

HETLIOZ® net product sales were $17.5 million in the third quarter of 2023

Fanapt® (iloperidone) tablets 1 mg, 2 mg, 4 mg, 6 mg, 8 mg, 10 mg, 12 mg

Fanapt® net product sales were $21.3 million in the third quarter of 2023

Strategic Focus

Increase revenue

Organically through existing products

Business development opportunities

Advance pipeline

Late / early-stage programs

Emerging ASO platform

Consumer focus

Increase access and affordability for patients

Engage directly with consumer

Commercial Priorities & Milestones

- Continued focus on market for schizophrenia
- Pursue FDA approval for Fanapt® in the indication of bipolar I disorder in adults
- Advance VHX-896 (formerly P88), as well as Long Acting Injectable (LAI)

- Retain market share despite generic competition through focus on patient loyalty
- Continue growth of HETLIOZ® in SMS in U.S. market
- Pursue approval of HETLIOZ® in SMS in the E.U. market
- Pursue FDA approvals for HETLIOZ® in the indications of insomnia and jet lag disorder

- Pursue FDA approval for tradipitant in patients with gastroparesis
- Advance motion sickness program

Fanapt® for Schizophrenia:

Fanapt® (iloperidone) tablets
1 mg, 2 mg, 4 mg, 6 mg, 8 mg, 10 mg, 12 mg

- About 1% of adult population worldwide is diagnosed with schizophrenia[1]
- About 3 million people in the U.S. live with schizophrenia

Akathisia
Frequently seen with antipsychotics

- Up to 25% of patients treated with some antipsychotics experience akathisia

- Patients frequently switch antipsychotic treatments due to side effects[2]
- Side effects include metabolic, weight and movement disorders

- Vanda owns global rights for Fanapt®
- Commercialized outside the U.S. through partners

1. NIMH.
2. Prescribing Information for leading brands.

HETLIOZ® for Non-24-Hour Sleep-Wake Disorder (Non-24)

Key demographics

Blind individuals with Non-24

~70% totally blind have Non-24[1]

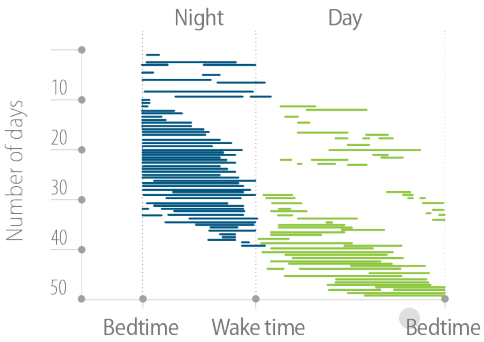
1:4000 in U.S. (~80,000)[2]

Sighted individuals with Non-24

Non-24 is comorbid with depressive and bipolar disorders[3]

Prevalence of Non-24 in the general population is unclear but appears rare in sighted individuals[3]

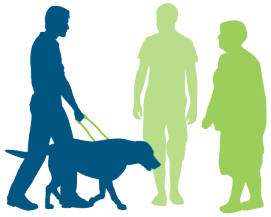
Misaligned circadian timing system



Clinical characteristics

Disrupted nighttime sleep

Excessive daytime sleepiness



Poor social and occupational functioning

1. Dressman et al. Seventy Percent of Totally Blind People with Sleep Complaints Are Not Entrained to the 24 Hour Clock. SLEEP Conference 2012. Vanda Pharmaceuticals Inc. June 2012.
2. Vanda estimate.
3. Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM-5), American Psychiatric Association, March 2013, page 396-397.

HETLIOZ® for Smith-Magenis Syndrome (SMS)

- **HETLIOZ® first approved treatment for nighttime sleep disturbances in SMS (December 2020)**
- **Pursuing approval in the E.U. market**
- **Severe sleep disorder is the strongest predictor of maladaptive behavior**

1/15,000-25,000 births in the U.S.[1,2]

Chromosomal deletion of 17p11.2 Rare mutations of the retinoic acid 1 (RAI1) gene

Major physical, developmental & behavioral features

Hetlioz® (tasimelteon) capsules 20 mg

Hetlioz LQ® (tasimelteon) Oral Suspension 4mg/mL

1. Orphanet ORPHA number 819.
2. Smith et al. GeneReviews. 2001.

HETLIOZ® for Smith-Magenis Syndrome (SMS)

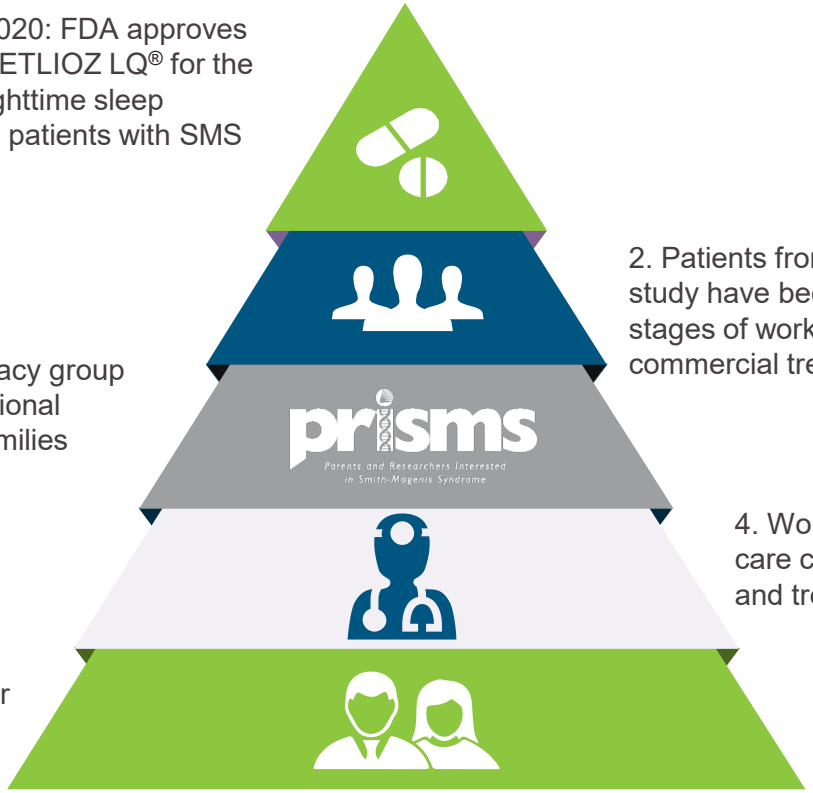
Hetlioz® (tasimelteon) capsules 20 mg

Hetlioz LQ® (tasimelteon) Oral Suspension 4mg/mL

1. December 2020: FDA approves HETLIOZ® & HETLIOZ LQ® for the treatment of nighttime sleep disturbances in patients with SMS

2. Patients from the ongoing open label clinical study have been contacted and are at different stages of working with their doctors to begin commercial treatment

3. In collaboration with the advocacy group PRISMS, we are contacting additional individuals with SMS and their families



4. Work with diagnostic centers and tertiary care clinics where patients seek diagnosis and treatment

5. Targeted and direct-to-consumer advertising for individuals with SMS, their families and their treating physicians

Research and Development

Clinical Development Pipeline

Product	Indication	Preclinical	Phase I	Phase II	Phase III	Regulatory
Hetlioz® (tasimelteon) capsules 20 mg	Jet Lag Disorder					
	Insomnia					
	Delayed Sleep Phase Disorder (DSPD)					
	Non-24 Pediatric					
Fanapt® (iloperidone) tablets 1 mg, 2 mg, 4 mg, 6 mg, 8 mg, 10 mg, 12 mg	Bipolar I Disorder					
	Long Acting Injectable (LAI)					
VHX-896	Schizophrenia					
	Bipolar I Disorder					
Tradipitant	Gastroparesis					
	Motion Sickness					
	Atopic Dermatitis					
VTR-297	Hematologic Malignancies					
CFTR	VSJ-110 (Activator)					
	VPO-227 (Inhibitor)					
VQW-765	Social/Performance Anxiety					

HETLIOZ® Lifecycle Management

HETLIOZ® Lifecycle Management Programs

Hetlioz® (tasimelteon) capsules 20 mg

Hetlioz LQ® (tasimelteon) Oral Suspension 4mg/mL

1 Jet Lag Disorder

- Clinical program completed

2 Insomnia

- Clinical program completed; sNDA accepted for filing with PDUFA target action date of 3/4/2024

3 Delayed Sleep Phase Disorder

- Phase III program initiated

4 Non-24 Pediatric

- Phase III clinical program in preparation

Jet Lag Disorder

HETLIOZ® for Jet Lag Disorder

U.S. Traveler Demographics

Over 20 million U.S. residents travel to destinations in Europe, the Middle East and Asia each year.[1]

78% of transmeridian travelers experience sleep disturbances.[2]

80% of U.S. passengers traveling 5-8 time zones pass through 10 airports. 35% through JFK and Newark.[3]

1. US Department of Commerce, International Trade Administration, National Travel & Tourism Office. Profile of U.S. Residents Travelers Visiting Overseas Destinations: 2015 Outbound.
2. Cho K, Ennaceur A, Cole C, Suh C. Chronic jet lag produces cognitive deficits. J Neuroscience 20:RC66 (2000).
3. Bureau of Transportation Statistics. Air Carriers: T-100 International Market (all carriers). August 2017.

Jet Lag Disorder – JET8 Study Results

Results reported in March 2018

- The magnitude of the total sleep time benefit of 85 minutes improvement over placebo is significant and clinically meaningful
- The demonstration of benefits in measurements of next day alertness on both KSS and VAS is meaningful and it underscores the ability of HETLIOZ® to address both nighttime and daytime symptoms of jet lag disorder

Assessment	Endpoint	HETLIOZ®	Placebo	Difference	p-value Summary
PSG (minutes)	TST 2/3*	216.4	156.1	60.3	p<0.0001
	TST Full	315.8	230.3	85.5	p<0.0001
	LPS	21.8	36.8	-15.1	p<0.01
	WASO	144.6	219.1	-74.6	p<0.0001
KSS (1-9)	Average	4.0	4.5	-0.5	p<0.01
VAS (0-100)	Average	60.8	54.2	6.6	p<0.01

Abbreviations

PSG	Polysomnography
TST	Total Sleep Time
LPS	Latency to Persistent Sleep
WASO	Wake After Sleep Onset
KSS	Karolinska Sleepiness Scale
VAS	Visual Analog Scale

Jet Lag Disorder – Clinical Program

4 Positive Clinical Studies

Study	Patients	Design
JET8 (3107)	318	Circadian challenge of an 8-hour advance to a subject's usual bedtime
JET5 (3101)	411	Circadian challenge of a 5-hour advance to a subject's usual bedtime
JET	25	A two-phase transatlantic travel study, with an observational travel phase (baseline) followed by a treatment phase
2101 study	39	HETLIOZ® shifted circadian rhythms on the first night

Regulatory Status:

- **Vanda received a complete response letter (CRL) from the FDA in August 2019 related to the sNDA of HETLIOZ® for the treatment of jet lag disorder**
- **Vanda is continuing to pursue a hearing with the Commissioner of FDA on the approvability of the jet lag sNDA**
- **Vanda believes the HETLIOZ® clinical data and safety profile support potential as a treatment option for jet lag disorder, and Vanda intends to continue to pursue regulatory approval of the sNDA**

Delayed Sleep Phase Disorder (DSPD)

HETLIOZ® for Delayed Sleep Phase Disorder (DSPD)

~ 3.3 million adults in the U.S.*

Prevalence

The prevalence of delayed sleep-wake phase disorder (DSPD) is highest in adolescents and young adults, with rates estimated between **3.3 and 4.6 percent**.[1]

The prevalence of DSPD in adults is lower, with estimates between **0.2 to 1.7 percent.**[1]

In a study of patients with Circadian Rhythm Sleep Disorders (CRSD), **83% were diagnosed with DSPD**.[2]

90% of those DSPD patients reported an onset of their symptoms during childhood or adolescence.[2]

DSPD is likely the most prevalent circadian-rhythm sleep disorder, **affecting ~1% of the population**, and 7–10% of patients with disorders of initiating or maintaining sleep.[3]

1. Up-to-Date – Delayed Sleep Phase Disorder
2. Dagan, Y, and Eisenstein, M. Circadian rhythm sleep disorders: toward a more precise definition and diagnosis. Chronobiology International 1999;16:213-22
3. P.J. Murphy, Delayed Sleep-Phase Type, Encyclopedia of Sleep, Academic Press, 2013, Pages 22-25, ISBN 9780123786111, https://doi.org/10.1016/B978-0-12-378610-4.00268-0.

** Based on estimate of approximately 1% of U.S. population*

Delayed Sleep Phase Disorder (DSPD) Symptoms & Clinical Expression

Delayed Sleep Onset

Individuals with DSPD habitually go to bed and wake-up significantly later than typical or desired times. DSPD patients have an inability to fall asleep at a conventional time.[1]

Sleep Insufficiency & Daytime Impairment

Delayed bedtime, combined with conventional school/work start times causes significant reductions in total sleep time for DSPD patients.

Circadian desynchronization in DSPD is akin to jet lag, individuals may have low energy in the daytime because they are attempting to be awake while sleep propensity is high.[1]

Clinical History

DSPD typically emerges during adolescence. Age-related circadian rhythm changes may lessen the propensity for delayed sleep in adulthood.[1]

Comorbidities

Comorbid depression is common among patients with DSPD.

A delayed circadian preference has been described in adults with bipolar I disorder, in some cases correlating with higher illness recurrence rates.[1]

1. *Up-to-Date – Delayed Sleep Phase Disorder*

Fanapt® Lifecycle Management

Fanapt® Lifecycle Management Programs

Fanapt® (iloperidone) tablets
1 mg, 2 mg, 4 mg, 6 mg, 8 mg, 10 mg, 12 mg

1 Bipolar I Disorder

- Phase III program complete; positive results announced in December 2022
- Pursuing FDA approval for Fanapt® in the indication of bipolar I disorder in adults; sNDA accepted for filing with PDUFA target action date of 4/2/2024

2 Long Acting Injectable

- Pharmacokinetic (PK) study of Fanapt® long-acting injectable formulation is ongoing and we are finalizing and optimizing dosing and administration
- A Phase III study of the long-acting injectable for acute schizophrenia treatment will follow the PK study

3 VHX-896 (formerly P88)

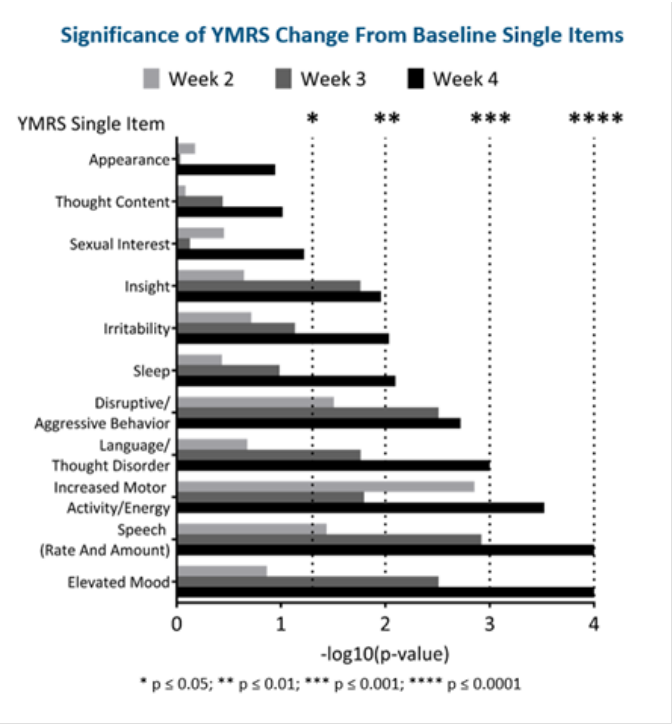
- VHX-896 is the active metabolite of iloperidone that we believe has the potential to improve the clinical profile of Fanapt® and create sustained, long-term value in the treatment of psychiatric disorders

Bipolar I Disorder

Fanapt® for Bipolar I Disorder

Results reported in December 2022

- The Phase III study enrolled approximately 400 volunteers with a history of bipolar I disorder suffering from a current episode of mania.
- The primary endpoint was assessed by the Young Mania Rating Scale (YMRS), a rating scale of clinical severity in the core symptoms of mania.
- Looking at the YMRS change from baseline at week 4, Fanapt® was significantly superior to placebo (p=0.000008).



Fanapt® for Bipolar I Disorder

Results reported in December 2022

- The secondary endpoints, Clinician Global Impression of Severity (CGI-S) and Clinician Global Impression of Change (CGI-C), also achieved statistical significance (p=0.0005 and p=0.0002, respectively) at week 4.

- Bipolar disorder is highly prevalent in the United States, estimated to affect 2.8%[1], of the U.S. adult population, a number approximately up to ten times higher than the estimated prevalence of schizophrenia[2,3].

- This pivotal study data of Fanapt® for the treatment of acute manic and mixed episodes associated with bipolar I disorder in adults included in supplemental New Drug Application (sNDA). Pursuing FDA approval for Fanapt® in the indication of bipolar I disorder in adults; sNDA accepted for filing with PDUFA target action date of 4/2/2024.

1. Harvard Medical School, 2007. National Comorbidity Survey (NSC). (2017, August 21). Retrieved from https://www.hcp.med.harvard.edu/ncs/index.php.
2. Kessler, R.C., Birnbaum, H., Demler, O., Falloon, I.R., Gagnon, E., Guyer, M., Howes, M.J., Kendler, K.S., Shi, L., Walters, E., Wu, E.Q. (2005). The prevalence and correlates of nonaffective psychosis in the National Comorbidity Survey Replication (NCS-R). Biological Psychiatry, 58(8), 668-76. doi: 10.1016/j.biopsych.2005.04.034
3. Wu, E.Q., Shi, L., Birnbaum, H., Hudson, T., Kessler, R. (2006). Annual prevalence of diagnosed schizophrenia in the USA: a claims data analysis approach. Psychological Medicine, 36(11), 1535-40. doi: 10.1017/S0033291706008191

Tradipitant Programs

Tradipitant Programs

1 Gastroparesis

- Phase III study results reported in February 2022; 12-week study of ~200 patients with idiopathic or diabetic gastroparesis
- Phase II positive study with results reported in December 2018 and published in Gastroenterology in January 2021
- Pursuing FDA approval for tradipitant in patients with gastroparesis

2 Motion Sickness

- Second Phase III study initiated
- First Phase III positive study results reported in May 2023
- Phase II positive study results reported in July 2019

3 Atopic Dermatitis

- EPIONE 2 Phase III study on hold
- EPIONE Phase III study results reported in February 2020

Gastroparesis

Tradipitant for Gastroparesis

- **Completed two clinical studies of tradipitant in gastroparesis. Pursuing FDA approval for tradipitant in patients with gastroparesis.**
- **Gastroparesis is a significant unmet medical need.**
- **Last treatment approved more than 40 years ago[1].**

600,000 diagnosed

600,000 people estimated to be diagnosed in the U.S.[2]

300,000 prescriptions

Appx. 300,000 metoclopramide prescriptions per month.[3]

6 million people

Estimated U.S. prevalence of 1.8% of the population.[2]

1. Reglan (metoclopramide) initial FDA approval 1979.
2. Rey et al J Neurogastroenterol Motil, Jan 2012.
3. IQVIA Prescription Data

Gastroparesis – Symptoms & Clinical Expression[1]

Diabetic or Idiopathic Gastroparesis

Chronic Nausea

Patients with gastroparesis suffer from chronic, severe and debilitating nausea.

Vomiting

Gastroparesis can cause vomiting, which can lead to weight loss and hospitalization due to nutritional deficiencies.

Delayed Gastric Emptying

Many patients with gastroparesis have a mechanical defect of delayed gastric emptying, which may be the cause of some of their symptoms.

Additional GI Symptoms

Patients with gastroparesis may also experience postprandial fullness, early satiety and abdominal pain.

1. Carlin, J. L., Lieberman, V. R., Dahal, A., Keefe, M. S., Xiao, C., Birznieks, G., Abell, T. L., Lembo, A., Parkman, H., & Polymeropoulos, M. H. (2020). Efficacy and safety of tradipitant in patients with diabetic and idiopathic gastroparesis in a randomized, placebo-controlled trial. Gastroenterology. Advance online publication. https://doi.org/10.1053/j.gastro.2020.07.029

Tradipitant Gastroparesis Clinical Program

1 Phase II Study (VP-VLY-686-2301)

- 4-week study of approximately 150 adult patients with diabetic or idiopathic gastroparesis
- Tradipitant was shown to be effective in improving nausea and overall symptoms in patients with gastroparesis
- Efficacy established by tradipitant in the 4-week double-blind phase was persistent in the open-label phase

2 Phase III Study (VP-VLY-686-3301)

- 12-week study of approximately 200 adult patients with diabetic or idiopathic gastroparesis
- The study did not meet its primary endpoint; however, when accounting for confounders, strong evidence of drug effect across a number of symptoms was observed
- Open-label phase remains open with over 300 patients already enrolled

3 Expanded Access Program

- Vanda initiated an expanded access program for patients requesting access to tradipitant outside of the clinical studies
- Vanda continues to receive requests from patients reaching out to gain access to tradipitant through the Expanded Access program, which has multiple patients continuing to take tradipitant for more than a year

Gastroparesis – Phase II Study

Results reported in December 2018, published in *Gastroenterology* January 2021[1]

Study Design

- 4 weeks of double-blind treatment followed by optional 8 weeks of open-label treatment
- 85 mg b.i.d.
- 47 study sites in the U.S.

Population

- Approximately 150 randomized subjects
- Stratified by idiopathic or diabetic gastroparesis

Assessments

- Patient Reported Daily Diary: Nausea, Vomiting & Other Symptoms
- Patient Assessment of GI Disorders (PAGI-SYM)
- Patient Global Impression (PGI-C)
- Clinical Global Impression (CGI-S)

1. Carlin, J. L., Lieberman, V. R., Dahal, A., Keefe, M. S., Xiao, C., Birznieks, G., Abell, T. L., Lembo, A., Parkman, H., & Polymeropoulos, M. H. (2020). Efficacy and safety of tradipitant in patients with diabetic and idiopathic gastroparesis in a randomized, placebo-controlled trial. Gastroenterology. Advance online publication. https://doi.org/10.1053/j.gastro.2020.07.029

Gastroparesis – Phase III Study

Study is complete and results were reported in February 2022

Study Design

- 12 weeks of double-blind treatment
- 85 mg b.i.d.
- 40 study sites in the U.S.

Population

- Approximately 200 randomized subjects
- Stratified by idiopathic or diabetic gastroparesis

Assessments

- Patient Reported Daily Diary: Nausea, Vomiting & Other Symptoms
- Patient Assessment of GI Disorders (PAGI-SYM)
- Patient Global Impression (PGI-C)
- Clinical Global Impression (CGI-S)

Gastroparesis – Pooled Study Results

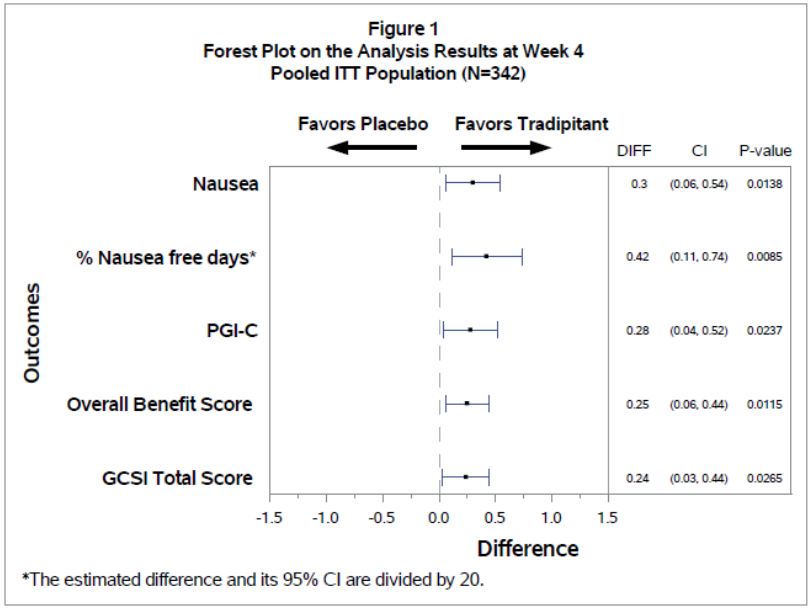
- Vanda completed a pooled analysis of two clinical studies of tradipitant in gastroparesis.
  - Population of 342 patients with relevant clinical endpoints.
  - Both studies were large multi-site, randomized, double-blind, placebo-controlled studies

- Tradipitant was shown to be superior to placebo in key clinical parameters:
  - Daily Diary-Nausea (primary endpoint parameter)
  - % Nausea Free Days
  - Patient Global Impression scale change (PGI-C)
  - Overall Benefit Score and Gastroparesis Cardinal Symptom Index (GCSI) score

- Both studies demonstrate the efficacy of tradipitant in relieving symptoms of gastroparesis.

Gastroparesis – Pooled Study Results

Figure 1 and Table 1 show the results of such pooled analysis of all patients randomized in the two studies (intent to treat population, ITT) and Figure 2 and Table 2 show the results for the same parameters in the population of patients who were judged as compliant to treatment based on analysis of drug exposure (treatment compliant population).



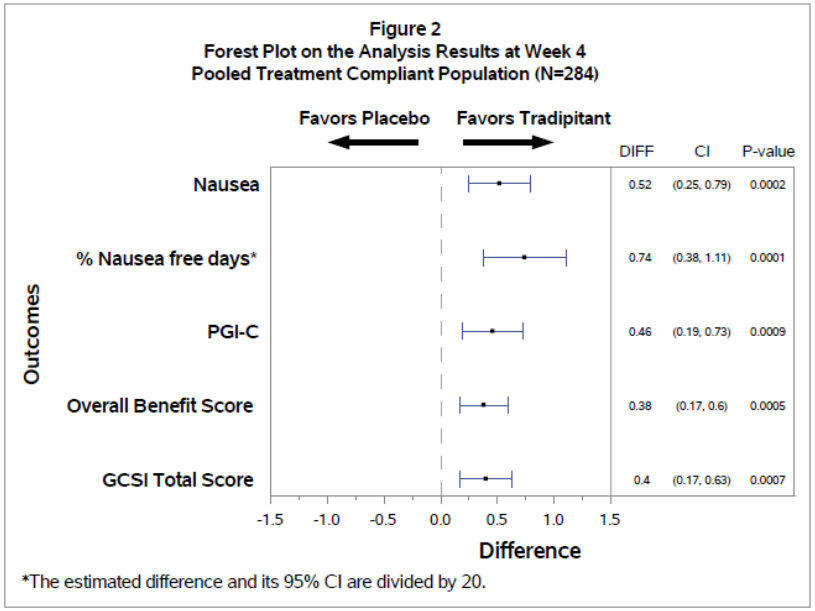


Table 1: Week 4 Pooled Analysis : ITT population for Study 1 and Study 2

	Tradipitant n=175	Placebo n=167	P-value
DD-Nausea	-1.15	-0.85	0.0138
% Nausea Free Days	20.96	12.52	0.0085
PGI-C	2.72	3.00	0.0237
Overall Benefit Score	1.13	0.88	0.0115
GCSI	-0.99	-0.76	0.0265

Table 2: Week 4 Pooled Analysis: Treatment Compliant Population for Study 1 and Study 2

	Tradipitant n=117	Placebo n=167	P-value
DD-Nausea	-1.37	-0.85	0.0002
% Nausea Free Days	27.44	12.58	0.0001
PGI-C	2.53	2.99	0.0009
Overall Benefit Score	1.27	0.88	0.0005
GCSI	-1.15	-0.75	0.0007

Motion Sickness

Tradipitant for Motion Sickness

Neurokinin-1 (NK-1) receptor antagonists have the potential to be effective in improving the symptoms of motion sickness, given the involvement of substance P in nauseogenic and emetic pathways and the expression of NK-1 receptors in the gastrointestinal system.[1]

Nausea and vomiting are the core symptoms of motion sickness[2]

The sensory mismatch resulting in motion sickness is due to discordance between actual and expected movement as perceived by the visual, vestibular, and kinesthetic systems[3]

About 2 to 3 million doses of Dramamine are purchased each month in the U.S.[4]

1. Polymeropoulos VM, Czeisler MÉ, Gibson MM, Anderson AA, Miglo J, Wang J, Xiao C, Polymeropoulos CM, Birznieks G and Polymeropoulos MH (2020) Tradipitant in the Treatment of Motion Sickness: A Randomized, Double-Blind, Placebo-Controlled Study. Front. Neurol. 11:563373. doi: 10.3389/fneur.2020.563373
2. Golding JF. Motion sickness. In: Furman JM, Lempert T, editors. Handbook of Clinical Neurology. Amsterdam, Boston, Heidelberg, London, New York, Oxford, Paris, San Diego, San Francisco, Singapore, Sydney. Tokyo: Elsevier. (2016). p. 371–90.
3. Graybiel A, Knepton J. Sopite syndrome: a sometimes sole manifestation of motion sickness. Aviat Space Envrion Med. (1976) 47:873–82.
4. IQVIA data

Motion Sickness – Phase II Study Results

Results reported in July 2019, published in *Frontiers in Neurology* in September 2020[1]

- Tradipitant was shown to be effective in preventing motion sickness[1]
- An exploratory analysis was performed to evaluate the effects of tradipitant under "calm" and "rough" seas. Under "rough" sea conditions (seas above 1 meter):
  - 72.2% of the placebo treated patients vomited as compared to 15.8% of those treated with tradipitant
  - A significant effect was also seen under "rough" conditions in the MSSS Worst score

Motion Sifnos Phase II Study Results[1]

Single day sea travel in the Pacific Ocean

Patients with a history of motion sickness

170mg tradipitant versus placebo

Primary Endpoints:
- % Vomiting
- Worst MSSS - Motion Sickness Severity Scale

ITT = Intent to Treat

Endpoint	Tradipitant	Placebo	Difference	P-Value
ITT	N=63	N=63		
% Vomiting	17.5%	39.7%	22.2%	0.0039
Worst MSSS	3.40	3.75	0.35	0.2936
Calm Sea	N=44	N=45		
% Vomiting	18.2%	26.7%	8.5%	0.3123
Worst MSSS	3.4	3.32	-0.09	0.8271
Rough Sea	N=19	N=18		
% Vomiting	15.8%	72.2%	56.4%	0.0009
Worst MSSS	3.19	4.57	1.38	0.0235

1. Polymeropoulos VM, Czeisler MÉ, Gibson MM, Anderson AA, Miglo J, Wang J, Xiao C, Polymeropoulos CM, Birznieks G and Polymeropoulos MH (2020) Tradipitant in the Treatment of Motion Sickness: A Randomized, Double-Blind, Placebo-Controlled Study. Front. Neurol. 11:563373. doi: 10.3389/fneur.2020.563373

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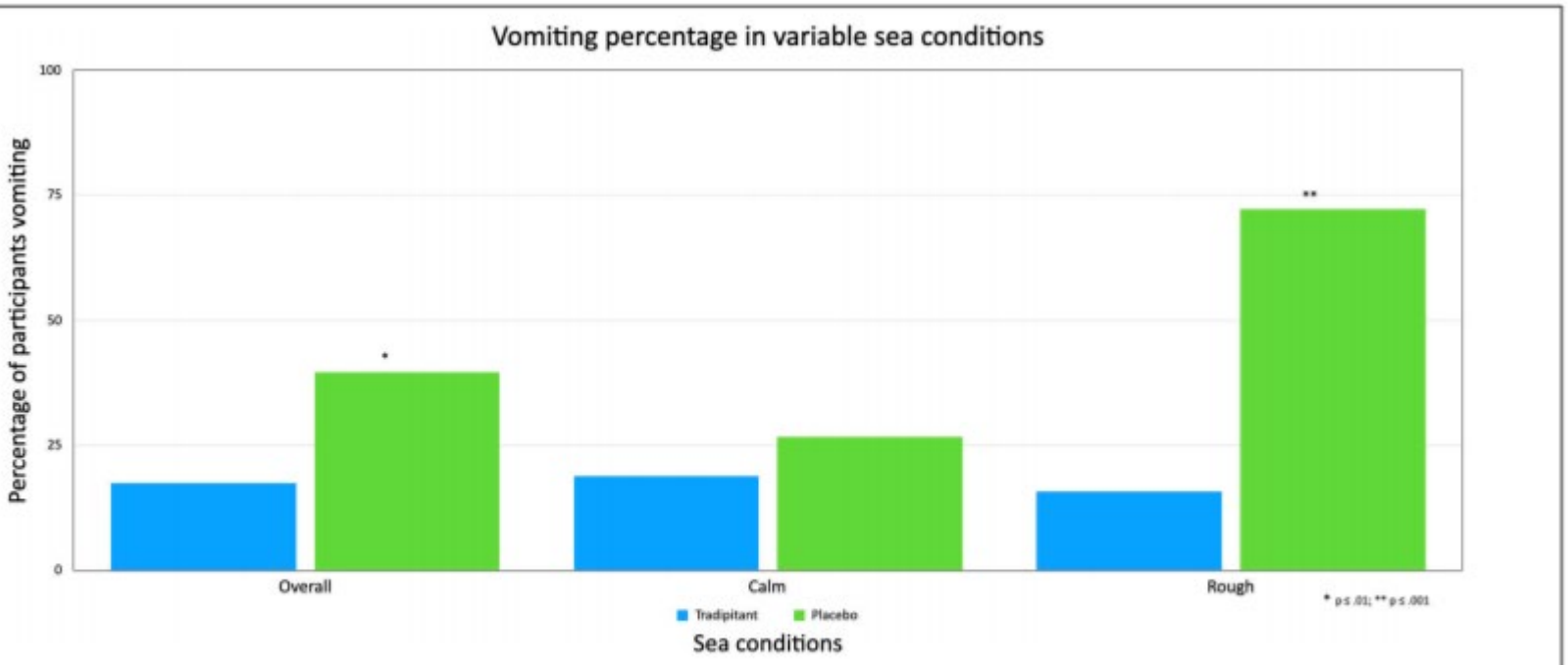


FIGURE 4 | Vomiting percentage in variable sea conditions. The figure reflects the percentage of participants vomiting (incidence of vomiting) across different sea conditions. A participant was considered as having vomited if they ever marked a score of 6 (vomiting) on the MSSS or vomited and elected to complete end of travel questionnaires before the end of travel.

1. *Polymeropoulos VM, Czeisler MÉ, Gibson MM, Anderson AA, Miglo J, Wang J, Xiao C, Polymeropoulos CM, Birznieks G and Polymeropoulos MH (2020) Tradipitant in the Treatment of Motion Sickness: A Randomized, Double-Blind, Placebo-Controlled Study. Front. Neurol. 11:563373. doi: 10.3389/fneur.2020.563373*

Motion Sickness: Phase III Program

- Phase III study completed – Positive results in prevention of vomiting
- Second Phase III study initiated
- Open label safety study started

Enrollment

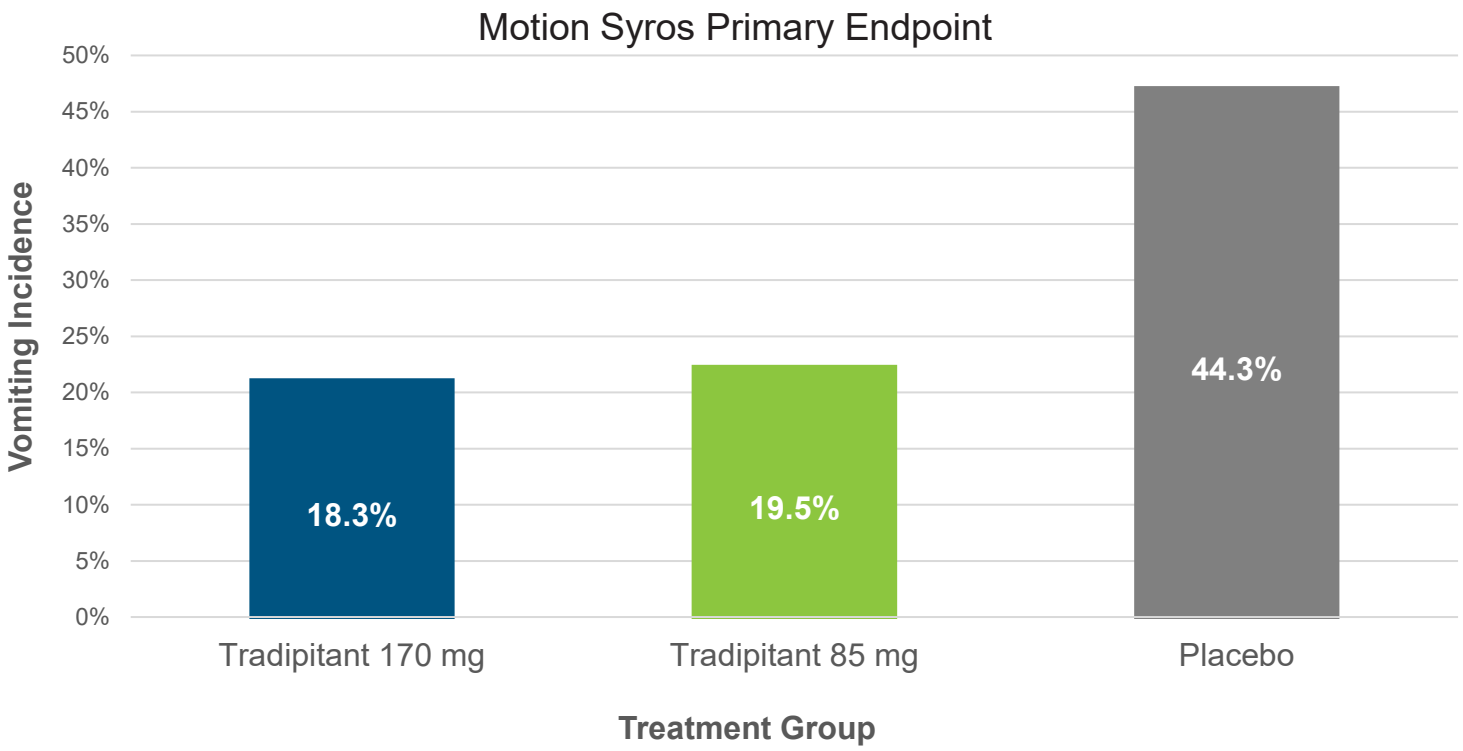
- First Phase III Study:
  - Randomized: 365
  - 85 and 170mg tradipitant both met primary endpoint preventing vomiting on the boats
- Second Phase III Study:
  - Similar study design

Program Timeline

- First Phase III results reported in May 2023
- Second Phase III study initiated
- Pursue FDA approval upon completion of clinical development program

Motion Sickness: Phase III Study

- 365 participant study across 34 boat trips in coastal waters of U.S. from November 2021 to April 2023
- Participants randomized 1:1:1 tradipitant 170mg v tradipitant 85mg v placebo 1 hour prior to departure
- Approximately 4-hour trips with questionnaires of vomiting and nausea every 30 minutes
- Incidence of vomiting was significantly lower in tradipitant 170mg (18.3%) and tradipitant 85mg (19.5%) as compared to placebo (44.3%), p < .0001



Atopic Dermatitis (AD)

Tradipitant for Atopic Dermatitis (AD)

- **Tradipitant has the potential to become a first line pharmacological treatment for patients with pruritus in AD in need of systemic treatment.**
- **Management of pruritus is a key treatment goal for patients.[1]**
- **Chronic pruritus, pruritus lasting more than 6 weeks, has been reported by 91% of AD patients.[2,3]**

~ 18 million people

Estimated U.S. prevalence of 17,800,000 people[4]

~ 6.4 million treated

Approximately 6.4 million drug-treated AD patients[5]

~ 10 million diagnosed

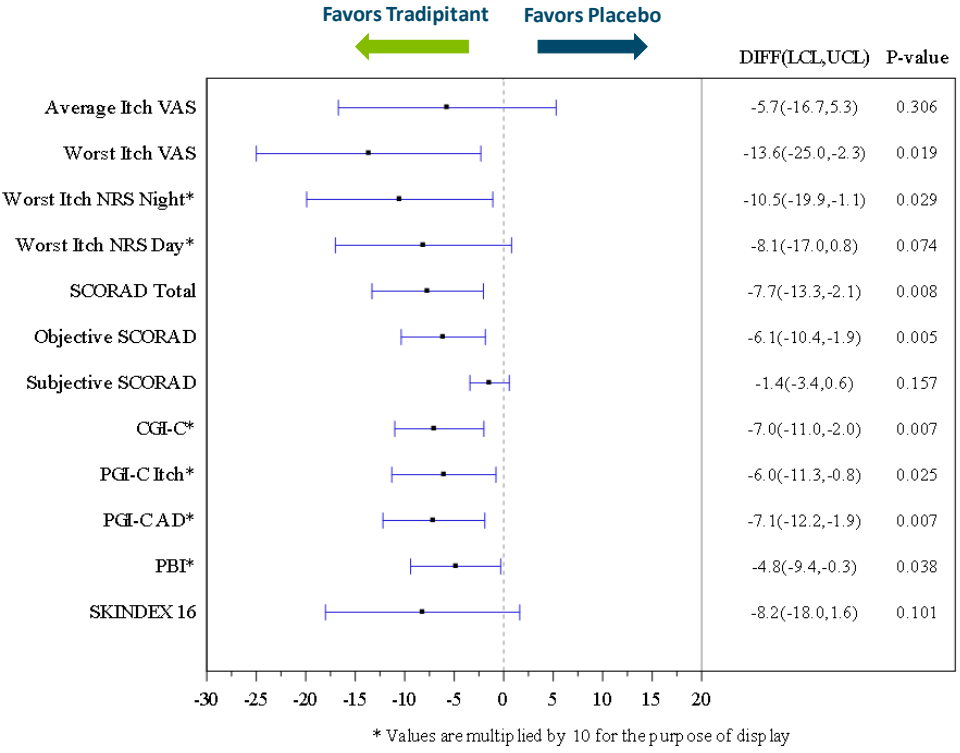
Approximately 9.8 million people diagnosed with AD[5]

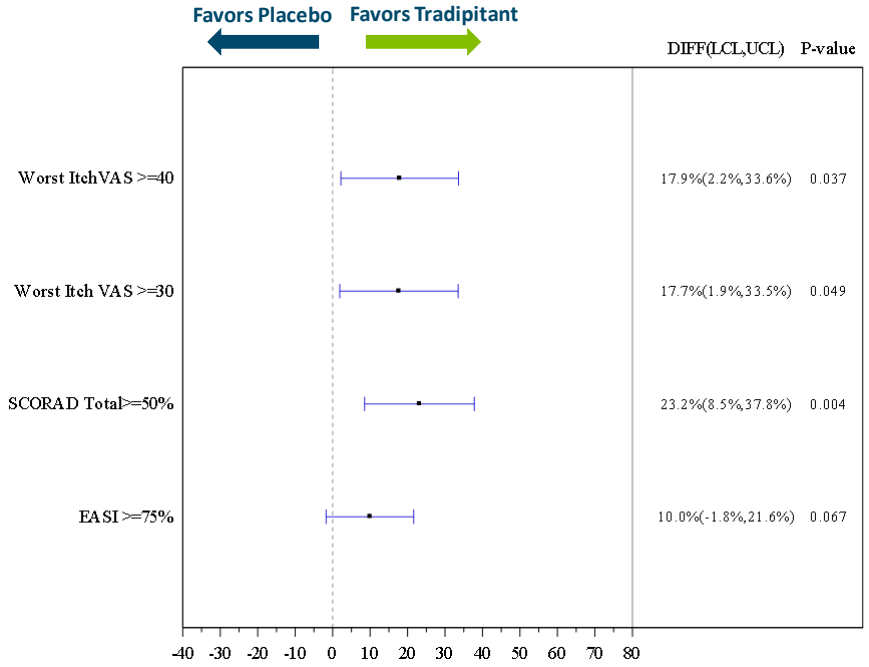
1. Adelphi – Atopic dermatitis Disease Specific Program – US 2014.
2. Dawn A, Papoiu ADP, Chan YH, Rapp SR, Rassette N, Yosipovitch G. Itch characteristics in atopic dermatitis: results of a web-based question-naire. Br J Dermatol 2009; 160: 642–644.
3. Mollanazar NK, Smi th PK, Yosipovitch G. Mediators of chronic pruritus in atopic dermatitis: getting the itch out? Clin Rev Allergy Immunol 2016; 51: 263–292.
4. National Eczema Association (2017).
5. Decision Resource Group, Atopic Dermatitis Landscape and Forecast (November 2015).

Atopic Dermatitis – Phase II Study Results

Results reported in September 2017

- Primary endpoint of average itch Visual Analog Scale (VAS) did not show significance due to high placebo effect and lack of sensitivity of this measure
- Significant improvements also shown in Clinical Global Impression scale (CGI-C), Patient Global Impression scale (PGI-C) and Patient Benefit Index (PBI)

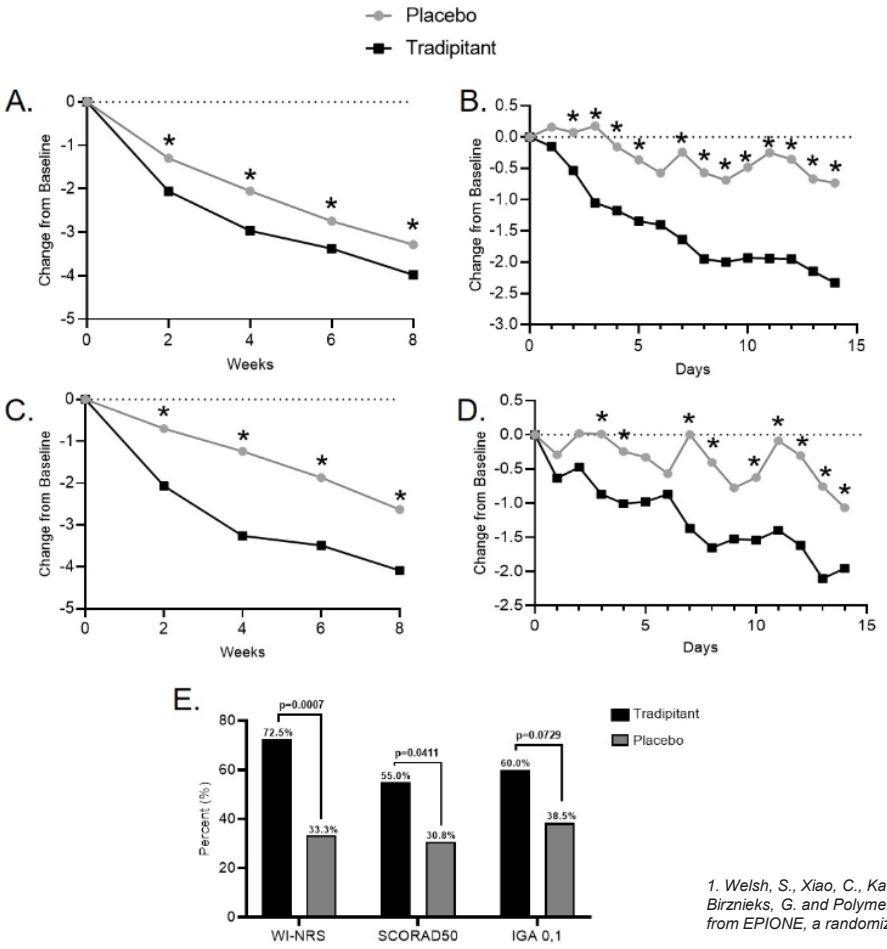




Atopic Dermatitis – Phase III Study Results

Results reported in February 2020, published in the *Journal of the European Academy of Dermatology and Venereology* in December 2020[1]

- **Tradipitant antipruritic effects not seen in moderate or severe AD and the study did not meet its primary endpoint**
- **Tradipitant significantly improved severe itch and nighttime sleep in patients with mild AD**
- **Pruritus improved in over 70% of patients with mild AD and seen after the first day of treatment**



A. Tradipitant treatment improved worst itch in mild AD.
B. Improvement in itch was observed after one full day of tradipitant treatment.
C. Tradipitant treatment improved sleep disturbance in mild AD.
D. Improvement in sleep was seen after two full days of tradipitant treatment.
E. A greater proportion of mild AD patients achieved success of four points or greater on WI-NRS and at least a 50% improvement on SCORAD.
A-D. P values are from MMRM analysis.
E. P values are from Fisher's exact test. *P < 0.05

1. Welsh, S., Xiao, C., Kaden, A., Brzezynski, J., Mohrman, M., Wang, J., Smieszek, S., Przychodzen, B., Ständer, S., Polymeropoulos, C., Birznieks, G. and Polymeropoulos, M. (2021), Neurokinin-1 receptor antagonist tradipitant has mixed effects on itch in atopic dermatitis: results from EPIONE, a randomized clinical trial. J Eur Acad Dermatol Venereol, 35: e338-e340. https://doi.org/10.1111/jdv.17090

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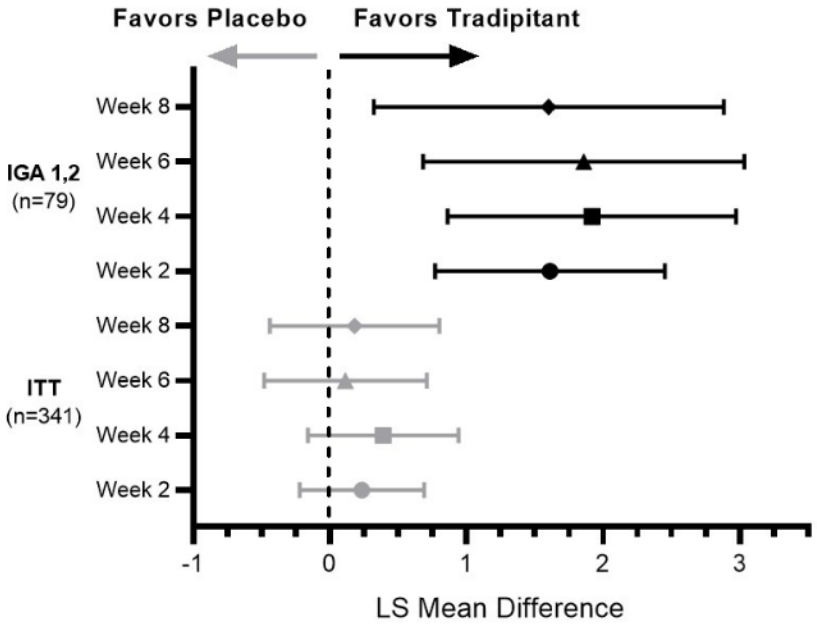
		DIFF (95% CI)
IGA 1,2 WI-NRS	Week 2	1.61 (0.77, 2.45)
	Week 4	1.92 (0.86, 2.97)
	Week 6	1.86 (0.68, 3.03)
	Week 8	1.60 (0.32, 2.88)
ITT WI-NRS	Week 2	0.23 (-0.22, 0.69)
	Week 4	0.39 (-0.16, 0.94)
	Week 6	0.11 (-0.48, 0.71)
	Week 8	0.18 (-0.44, 0.80)



Worst Itch NRS Change by Week. Mild AD patients have greater improvement in worst itch after tradipitant-treatment. Forest plots of the analysis of ITT and IGA 1,2 WI-NRS change by week. Plotted as LS Mean Difference and 95% CI after tradipitant or placebo treatment.

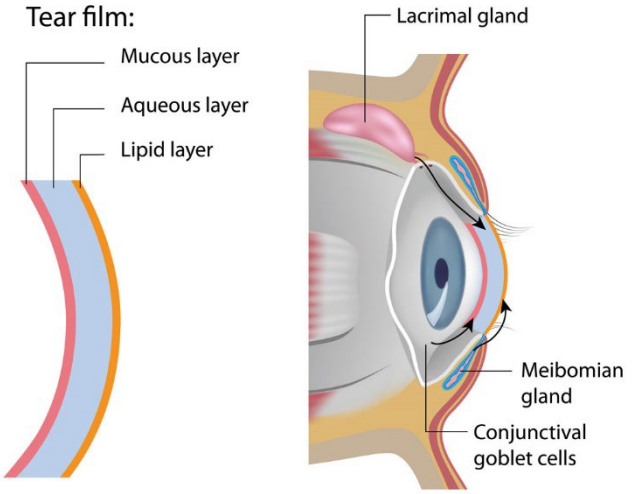
1. Welsh, S., Xiao, C., Kaden, A., Brzezynski, J., Mohrman, M., Wang, J., Smieszek, S., Przychodzen, B., Ständer, S., Polymeropoulos, C., Birznieks, G. and Polymeropoulos, M. (2021), Neurokinin-1 receptor antagonist tradipitant has mixed effects on itch in atopic dermatitis: results from EPIONE, a randomized clinical trial. J Eur Acad Dermatol Venereol, 35: e338-e340. https://doi.org/10.1111/jdv.17090

Early-Stage Programs

Early-Stage Programs

Cystic Fibrosis Transmembrane Conductance Regulators (CFTR)

- **VSJ-110** – CFTR Activator: VSJ-110 has shown efficacy in a dry eye model[1] and exhibited anti-inflammatory properties in both in vitro and in vivo assays
- Ongoing Phase II Conjunctivitis Study investigating anti-inflammatory effect of VSJ-110 (PDE4 inhibition) following ragweed ocular challenge
- **VPO-227** – CFTR Inhibitor: CFTR inhibitors decrease water secretion across epithelia, such as where aberrant CFTR activation occurs; they may be useful in the treatment of cholera, traveler's diarrhea, polycystic kidney disease, and other conditions of water hyper-secretion
- Cholera Disease: VPO-227 was granted Orphan Drug Designation by FDA for the treatment of cholera



Hematologic Malignancies

- VTR-297 is a histone deacetylase (HDAC) inhibitor
- Ongoing Phase II study of VTR-297 in Hematologic Malignancies at sites in the U.S. and Europe

Social/Performance Anxiety

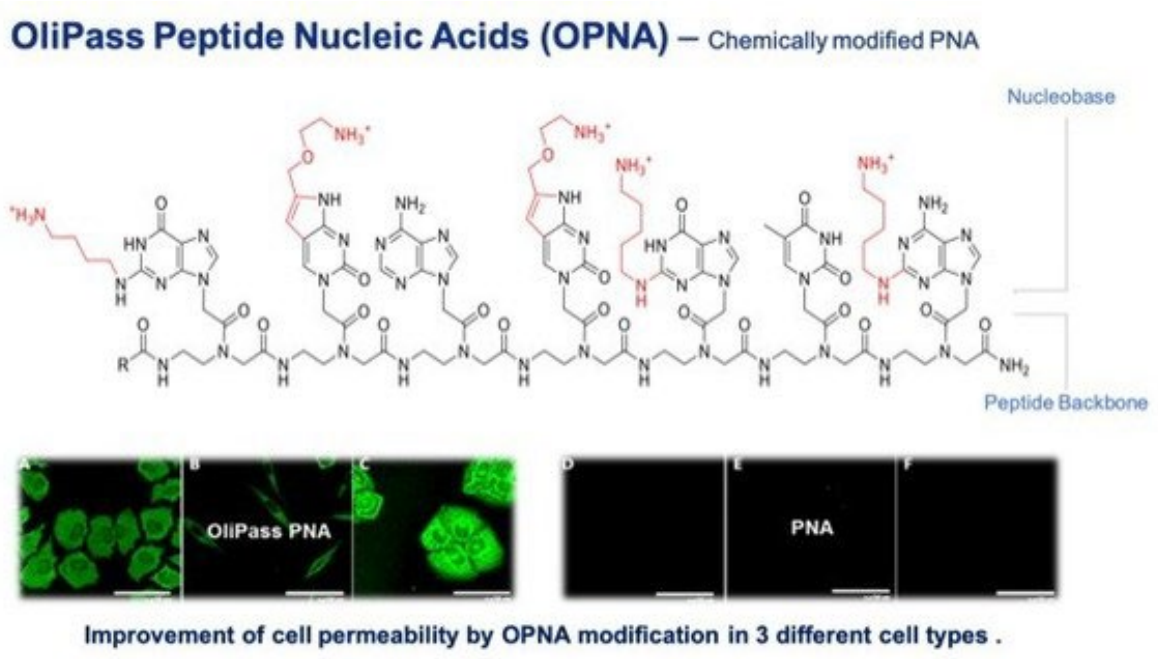
- VQW-765 is an Alpha-7 nicotinic acetylcholine receptor partial agonist
- Phase II study of a single-dose treatment to alleviate social/performance anxiety complete; results announced in December 2022

1. *Lee, S., P.W. Phuan, C.M. Felix, J.A. Tan, M.H. Levin and A.S. Verkman (2017). Nanomolar-potency aminophenyl-1,3,5-triazine activators of the cystic fibrosis transmembrane conductance regulator (CFTR) chloride channel for prosecretory therapy of dry eye diseases. J. Med. Chem. 60:1210-1218.*

Early-Stage Programs

Antisense Oligonucleotide (ASO)

- VCA-894A was granted Orphan Drug Designation for the treatment of Charcot-Marie-Tooth disease, axonal, type 2S (CMT2S), caused by cryptic splice site variants within IGHMBP2.
- In September 2022, Vanda and OliPass Corporation (OliPass) announced a research and development agreement to jointly develop a set of antisense oligonucleotide (ASO) molecules based on OliPass' proprietary modified peptide nucleic acids.
- This evolving discovery and development platform is intended to support Vanda's development of ASO-based precision medicine therapeutics.



Financial Results

2023 Financial Highlights

Q3 2023 Financial Highlights

$38.8 million

Total net product sales from HETLIOZ® and Fanapt® were $38.8 million in the third quarter of 2023

Hetlioz® (tasimelteon) capsules 20 mg

HETLIOZ® net product sales were $17.5 million in the third quarter of 2023

Fanapt® (iloperidone) tablets 1 mg, 2 mg, 4 mg, 6 mg, 8 mg, 10 mg, 12 mg

Fanapt® net product sales were $21.3 million in the third quarter of 2023

Financials – Results Through September 30, 2023

	Results Through September 30, 2023
HETLIOZ® Net Product Sales	$79.1M
Fanapt® Net Product Sales	$68.3M
Total Revenues	$147.4M
Cost of Goods Sold	$11.3M
Research & Development	$52.5M
Selling, General & Administrative	$89.3M
Intangible Asset Amortization	$1.1M
Operating Expenses	$154.2M
Net Income (Loss)	$4.9M
Cash[1]	$489.9M

1.Cash, cash equivalents and marketable securities

For more information on HETLIOZ®, please visit www.HETLIOZ.com

For more information on Fanapt®, please visit www.FANAPT.com


VANDA
PHARMACEUTICALS INC.