VERTEX

THE SCIENCE *of* POSSIBILITY

# VX-548 PHASE 3 RESULTS IN ACUTE PAIN

JANUARY 30, 2024

# SAFE HARBOR STATEMENT

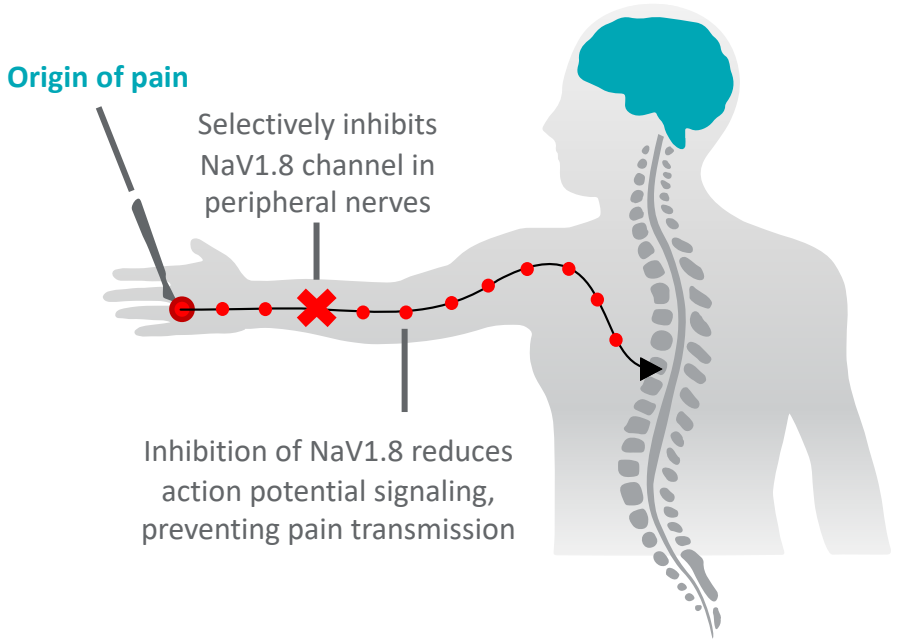
This presentation contains forward-looking statements as defined in the Private Securities Litigation Reform Act of 1995, as amended, including, without limitation, statements regarding our expectations for our pain program, our plans to file a New Drug Application for VX-548 with the U.S. FDA by mid-2024, our plans to secure a broad label for treatment of moderate to severe acute pain, our belief that the results support broad use of VX-548 in moderate to severe acute pain, our belief that a novel class of non-opioid pain signal inhibitors could transform the treatment of acute pain, starting with VX-548, and our plans to build out our commercial capabilities in pain, our expectations for the commercial potential for VX-548 as a treatment of moderate to severe acute pain. While Vertex believes the forward-looking statements contained in this presentation are accurate, these forward-looking statements represent the company's beliefs only as of the date of this presentation and there are a number of risks and uncertainties that could cause actual events or results to differ materially from those expressed or implied by such forward-looking statements. Those risks and uncertainties include, among other things, that our regulatory submissions may not be completed on the anticipated timeline, or at all, that we may not be able to achieve a broad label for VX-548, that data from the company's development programs may not support registration or further development of its potential medicines due to safety, efficacy or other reasons, and other risks listed under “Risk Factors” in Vertex's annual report filed with the Securities and Exchange Commission (SEC) and available through the company's website at www.vrtx.com and on the SEC’s website at www.sec.gov. You should not place undue reliance on these statements, or the scientific data presented. Vertex disclaims any obligation to update the information contained in this presentation as new information becomes available.

# POSITIVE RESULTS FOR VX-548 PIVOTAL PROGRAM IN ACUTE PAIN

**Continuing to build the body of evidence for VX-548:**

- ☑ Positive Phase 2 results:
  - Two acute pain studies - March 2022
- ☑ Positive Phase 2 results:
  - Diabetic Peripheral Neuropathy (DPN) study - Dec. 2023
  - 12-week dosing further supports overall safety profile
- ☑ Positive Phase 3 pivotal program results:
  - Three acute pain studies - January 2024

**First novel mechanism for acute pain in over 20 years**




**Vertex on track to file New Drug Application for VX-548 for moderate to severe acute pain in the U.S. by mid-2024; VX-548 has Fast Track & Breakthrough Therapy designations**

# POSITIVE RESULTS FROM OUR PIVOTAL PROGRAM SUPPORT BROAD, MODERATE TO SEVERE ACUTE PAIN INDICATION

- Both RCTs met primary endpoint with statistically significant improvement in pain compared to placebo
- Both RCTs showed clinically meaningful reduction in pain compared to baseline
- SASE study supported longer-term safety and effectiveness in broad range of acute pain conditions and settings
- VX-548 was safe and well tolerated in all three studies

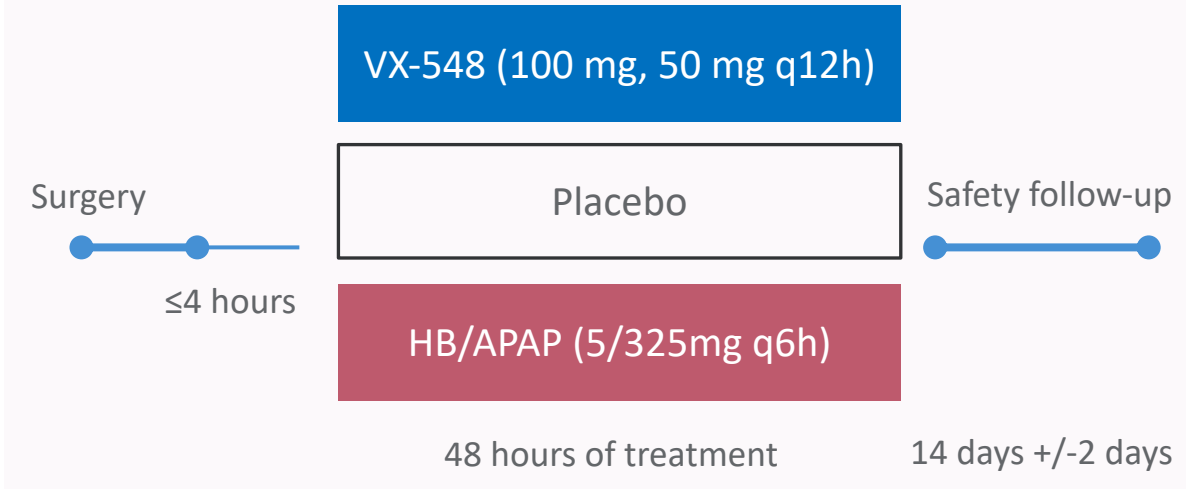
RCT = randomized controlled trial; SASE = single arm safety and effectiveness study

# VX-548 ACUTE PAIN PIVOTAL PROGRAM

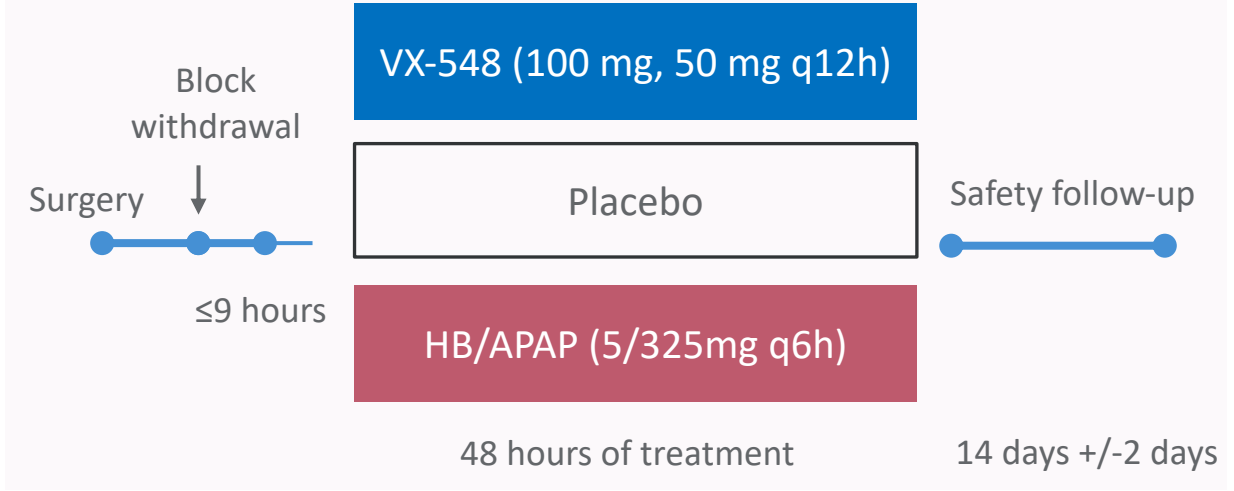
# VX-548 ACUTE PAIN PIVOTAL PROGRAM OVERVIEW

Two Phase 3 randomized, double-blind, placebo-controlled trials and a single arm safety and effectiveness study

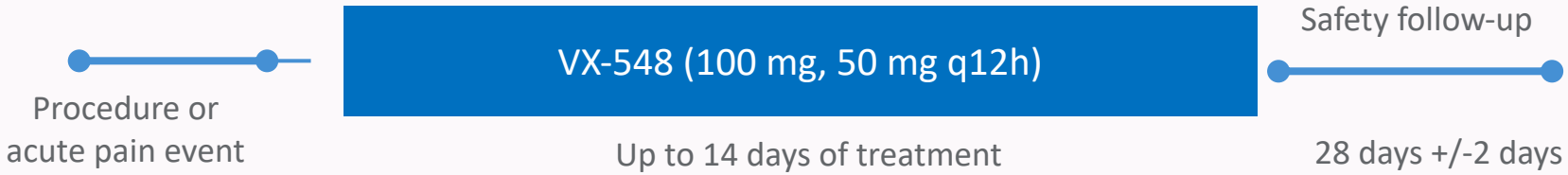
## 548-105 ABDOMINOPLASTY (N=1,118)




## 548-104 BUNIONECTOMY (N=1,073)




## 548-107 SINGLE ARM SAFETY & EFFECTIVENESS (SASE) STUDY (N=256)




**Randomization**: 2:1:2 VX-548, placebo, HB/APAP in each of the randomized controlled trials.

**Key inclusion criteria in RCTs**: patients ages 18 to 80 yrs, after abdominoplasty or bunionectomy surgery with moderate to severe pain, NPRS ≥ 4.

**Key inclusion criteria in SASE:** patients ages 18 to 80 yrs, with surgical or non-surgical pain that is moderate or severe, NPRS ≥ 4**.**

HB/APAP= hydrocodone bitartrate/ acetaminophen; q12h = every 12 hours; q6h = every 6 hours; RCTs = randomized controlled trials

# VX-548 ACUTE PAIN PIVOTAL PROGRAM OVERVIEW

Primary and key secondary endpoints

| 548-105 ABDOMINOPLASTY (N=1,118) | 548-104 BUNIONECTOMY (N=1,073) |
|---|---|

**Primary endpoint:**

Time-weighted sum of the pain intensity difference from 0 to 48 hours (SPID48) compared to placebo, recorded on the numeric pain rating scale (NPRS)

**Key Secondary endpoints:**

SPID48 compared to HB/APAP

Time to ≥2 point reduction in NPRS from baseline compared to placebo

## 548-107 SINGLE ARM SAFETY & EFFECTIVENESS (SASE) STUDY (N=256)

**Primary endpoint:**

Safety and tolerability

**Secondary endpoint**:

Patient global assessment (PGA) of VX-548 effectiveness at the end of treatment

# PHASE 3 RESULTS WITH VX-548 FOLLOWING ABDOMINOPLASTY SURGERY

# TREATMENT WITH VX-548 SHOWED STATISTICALLY SIGNIFICANT PAIN RELIEF COMPARED TO PLACEBO FOLLOWING ABDOMINOPLASTY SURGERY

## Primary endpoint

**SPID48 VX-548 vs. placebo**

| 548-105 ABDOMINOPLASTY | | |
|---|---|---|
| | PLACEBO<br>N=223 | VX-548<br>100 mg, 50 mg q12h<br>N=447 |
| SPID48 LS mean (SE) | 70.1<br>(6.1) | 118.4<br>(4.3) |
| SPID48 LS mean difference from placebo | | **48.4** |
| 95% CI | | (33.6, 63.1) |
| *P* value vs. placebo | | <0.0001 |

SPID48 = time-weighted sum of the pain intensity difference (SPID) from 0 to 48 hours; LS = least squares; SE = standard error; CI = confidence interval; q12h = every 12 hours

# HYPOTHESIS THAT VX-548 IS SUPERIOR TO HYDROCODONE ACETAMINOPHEN WAS NOT SUPPORTED IN THIS TRIAL

## Key secondary endpoint #1

## SPID48 VX-548 vs. HB/APAP

| 548-105 ABDOMINOPLASTY | | |
|---|---|---|
| | HB/APAP<br>5 mg / 325 mg q6h<br>N=448 | VX-548<br>100 mg, 50 mg q12h<br>N=447 |
| SPID48 LS mean (SE) | 111.8<br>(4.3) | 118.4<br>(4.3) |
| SPID48 LS mean difference from HB/APAP | | **6.6** |
| 95% CI | | (-5.4, 18.7) |
| *P* value vs. HB/APAP | | 0.2781 |

SPID48 = time-weighted sum of the pain intensity difference (SPID) from first dose up to 48 hours; LS = least squares; SE = standard error; CI = confidence interval; HB/APAP = hydrocodone bitartrate/ acetaminophen; q6h = every 6 hours; q12h = every 12 hours

# RAPID TIME TO MEANINGFUL PAIN RELIEF WITH VX-548

**Key secondary endpoint #2**

**Time to ≥2 point reduction in NPRS from baseline compared to placebo** *(in minutes)*

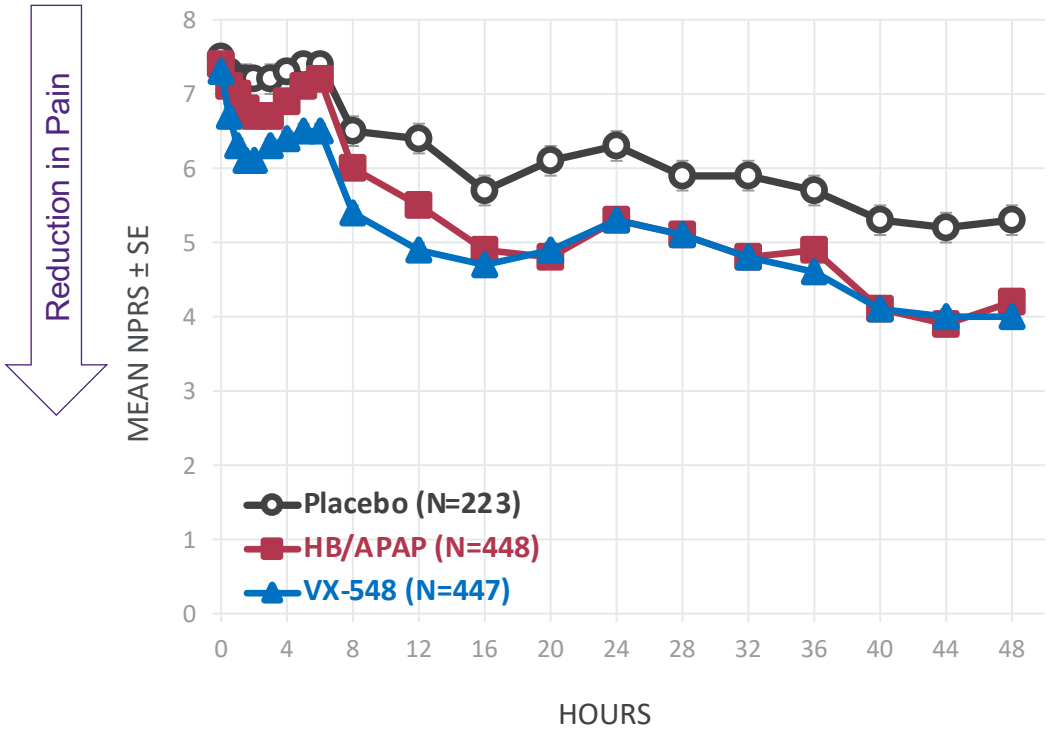
| 548-105 ABDOMINOPLASTY | | |
|---|---|---|
| | PLACEBO<br>N=223 | VX-548<br>100 mg, 50 mg q12h<br>N=447 |
| Median time to ≥2 point reduction in NPRS, 95% CI | **480 min**<br>(477, 705) | **119 min**<br>(90, 180) |
| *P* value vs. placebo | | <0.0001* |

* *Due to the break in hierarchical testing, P value is considered nominal.*

NPRS = numeric pain rating scale; CI = confidence interval; q12h = every 12 hours

# REDUCTION IN PAIN WITH VX-548 WAS RAPID, SUSTAINED OVER THE TREATMENT PERIOD AND CLINICALLY MEANINGFUL

## 548-105 ABDOMINOPLASTY
**Mean NPRS scores over the treatment period**




## 548-105 ABDOMINOPLASTY
**Reduction in pain scores at 48 hours of treatment**

| | PLACEBO N=223 | HB/APAP 5 mg / 325 mg q6h N=448 | VX-548 100 mg, 50 mg q12h N=447 |
|---|---|---|---|
| Baseline NPRS, mean | 7.5 | 7.4 | 7.3 |
| Change from baseline in NPRS, mean | -2.3 | -3.2 | **-3.4** |
| % reduction from baseline in mean NPRS | 31% | 43% | **47%** |

NPRS = numeric pain rating scale; HB/APAP = hydrocodone bitartrate/ acetaminophen; q6h = every 6 hours; q12h = every 12 hours

# VX-548 WAS SAFE AND WELL TOLERATED IN >1,000 PATIENT TRIAL FOLLOWING ABDOMINOPLASTY SURGERY

- Majority of adverse events (AEs) with VX-548 were mild or moderate in severity
- There were no serious adverse events (SAEs) related to VX-548
- In general, AEs were consistent with the post-surgical setting
- In the VX-548 arm, the incidence of AEs was lower than placebo*

| | 548-105 ABDOMINOPLASTY | | |
|---|---|---|---|
| | **Placebo N = 222 n (%)** | **HB/APAP N = 448 n (%)** | **VX-548 N = 448 n (%)** |
| **Subjects with any AEs** | 125 (56.3) | 272 (60.7) | 224 (50.0) |
| Common AEs, incidence ≥5% in any treatment arm | | | |
| Nausea | 56 (25.2) | 147 (32.8) | 85 (19.0) |
| Constipation | 24 (10.8) | 39 (8.7) | 47 (10.5) |
| Headache | 11 (5.0) | 32 (7.1) | 19 (4.2) |
| Dizziness | 17 (7.7) | 24 (5.4) | 18 (4.0) |
| Hypotension | 15 (6.8) | 16 (3.6) | 11 (2.5) |

The rate of SAEs in the abdominoplasty trial was low and SAEs were typical of subjects following the procedure; none were related to VX-548.

HB/APAP = hydrocodone bitartrate / acetaminophen 5 mg/325 mg every 6 hours; VX-548 is 100 mg first dose, 50 mg every 12 hours

*Incidence of subjects with any AEs is 50.0% in the VX-548 arm and 56.3% in the placebo arm.

# PHASE 3 RESULTS WITH VX-548 FOLLOWING BUNIONECTOMY SURGERY

# TREATMENT WITH VX-548 SHOWED STATISTICALLY SIGNIFICANT PAIN RELIEF COMPARED TO PLACEBO FOLLOWING BUNIONECTOMY SURGERY

## Primary endpoint

**SPID48 VX-548 vs. placebo**

| 548-104 BUNIONECTOMY | | |
|---|---|---|
| | PLACEBO<br>N=216 | VX-548<br>100 mg, 50 mg q12h<br>N=426 |
| SPID48 LS mean (SE) | 70.6<br>(6.3) | 99.9<br>(4.5) |
| SPID48 LS mean difference from placebo | | **29.3** |
| 95% CI | | (14.0, 44.6) |
| *P* value vs. placebo | | 0.0002 |

SPID48 = time-weighted sum of the pain intensity difference (SPID) from 0 to 48 hours; LS = least squares; SE = standard error; CI = confidence interval; q12h = every 12 hours

# HYPOTHESIS THAT VX-548 IS SUPERIOR TO HYDROCODONE ACETAMINOPHEN WAS NOT SUPPORTED IN THIS TRIAL

## Key secondary endpoint #1

## SPID48 VX-548 vs. HB/APAP

| 548-104 BUNIONECTOMY | | |
|---|---|---|
| | HB/APAP<br>5 mg / 325 mg q6h<br>N=431 | VX-548<br>100 mg, 50 mg q12h<br>N=426 |
| SPID48 LS mean (SE) | 120.1<br>(4.5) | 99.9<br>(4.5) |
| SPID48 LS mean difference from HB/APAP | | **-20.2** |
| 95% CI | | (-32.7, -7.7) |
| *P* value vs. HB/APAP | | 0.0016 |

SPID48 = time-weighted sum of the pain intensity difference (SPID) from first dose up to 48 hours; LS = least squares; SE = standard error; CI = confidence interval; HB/APAP = hydrocodone bitartrate / acetaminophen; q6h = every 6 hours; q12h = every 12 hours

# RAPID TIME TO MEANINGFUL PAIN RELIEF WITH VX-548

## Key secondary endpoint #2

**Time to ≥2 point reduction in NPRS from baseline compared to placebo**
*(in minutes)*

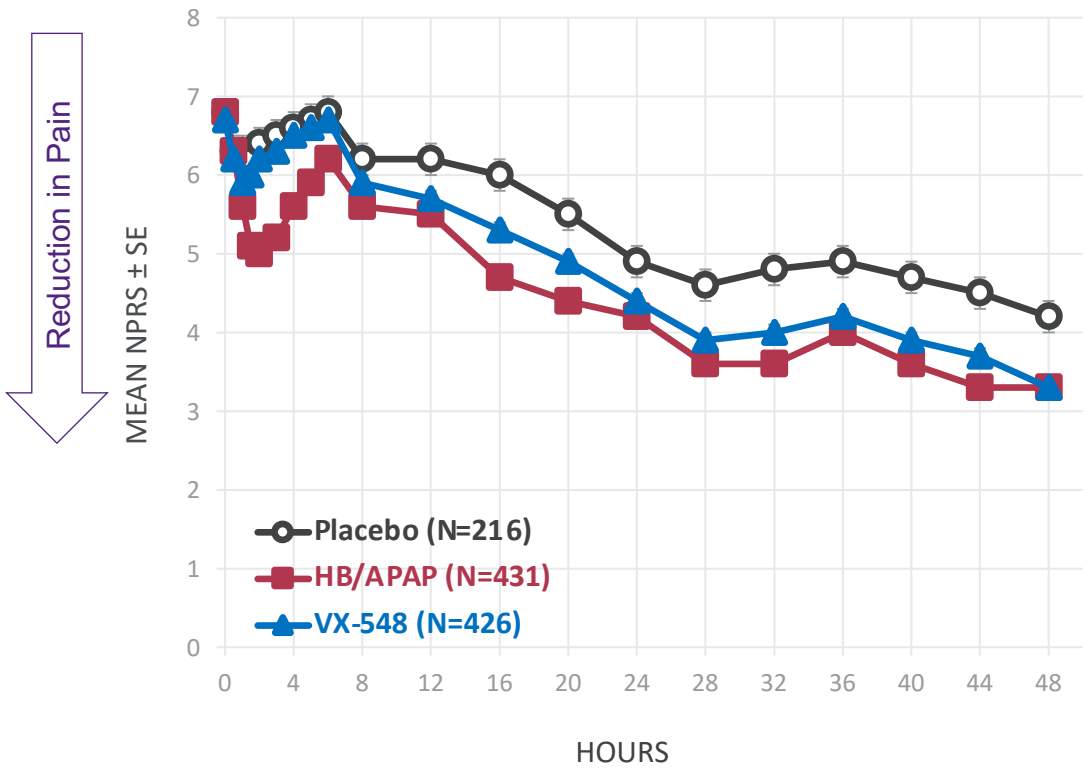
| 548-104 BUNIONECTOMY | | |
|---|---|---|
| | PLACEBO<br>N=216 | VX-548<br>100 mg, 50 mg q12h<br>N=426 |
| Median time to ≥2 point reduction in NPRS, 95% CI | **480 min**<br>(476, 716) | **240 min**<br>(117, 477) |
| *P* value vs. placebo | | 0.0016* |

* *Due to the break in hierarchical testing, P value is considered nominal.*

NPRS = numeric pain rating scale; CI = confidence interval; q12h = every 12 hours

# REDUCTION IN PAIN WITH VX-548 WAS RAPID, SUSTAINED OVER THE TREATMENT PERIOD AND CLINICALLY MEANINGFUL

## 548-104 BUNIONECTOMY
**Mean NPRS scores over the treatment period**




## 548-104 BUNIONECTOMY
**Reduction in pain scores at 48 hours of treatment**

| | PLACEBO N=216 | HB/APAP 5 mg / 325 mg q6h N=431 | VX-548 100 mg, 50 mg q12h N=426 |
|---|---|---|---|
| Baseline NPRS, mean | 6.8 | 6.8 | 6.7 |
| Change from baseline in NPRS, mean | -2.6 | -3.6 | **-3.4** |
| % reduction from baseline in mean NPRS | 38% | 53% | **51%** |

NPRS = numeric pain rating scale; HB/APAP = hydrocodone bitartrate/ acetaminophen; q6h = every 6 hours; q12h = every 12 hours

# VX-548 WAS SAFE AND WELL TOLERATED IN >1,000 PATIENT TRIAL FOLLOWING BUNIONECTOMY SURGERY

- Majority of AEs with VX-548 were mild or moderate in severity
- There were no SAEs in this trial
- In general, AEs were consistent with the post-surgical setting
- In the VX-548 arm, the incidence of AEs was lower than placebo*

| | 548-104 BUNIONECTOMY | | |
|---|---|---|---|
| | **Placebo N = 216 n (%)** | **HB/APAP N = 431 n (%)** | **VX-548 N = 426 n (%)** |
| **Subjects with any AEs** | 76 (35.2) | 180 (41.8) | 132 (31.0) |
| Common AEs, incidence ≥5% in any treatment arm | | | |
| Nausea | 23 (10.6) | 62 (14.4) | 35 (8.2) |
| Headache | 20 (9.3) | 45 (10.4) | 21 (4.9) |
| Constipation | 9 (4.2) | 22 (5.1) | 15 (3.5) |
| Dizziness | 11 (5.1) | 23 (5.3) | 15 (3.5) |

HB/APAP = hydrocodone bitartrate / acetaminophen 5 mg/325 mg every 6 hours; VX-548 is 100 mg first dose, 50 mg every 12 hours
*Incidence of subjects with any AEs is 31.0% in the VX-548 arm and 35.2% in the placebo arm.

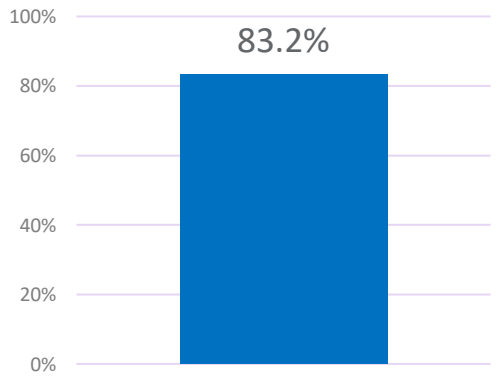
# RESULTS WITH VX-548 FROM THE SINGLE ARM SAFETY AND EFFECTIVENESS (SASE) TRIAL

# SASE TRIAL RESULTS SUPPORT LONGER-TERM SAFETY AND EFFECTIVENESS IN BROAD SURGICAL AND NON-SURGICAL POPULATION

- VX-548 was safe and well tolerated in a broad range of surgical and non-surgical pain conditions treated up to 14 days

| **548-107 Single Arm Safety & Effectiveness Trial**<br>Common adverse events, incidence ≥5% | **Total**<br>**N = 256**<br>**n (%)** |
|---|---|
| **Subjects with AEs** | **94 (36.7)** |
| Headache | 18 (7.0) |

- Over 80% of patients rated their experience as Good, Very Good or Excellent on the Patient Global Assessment (PGA)




**Surgical patients* (N=222)**

- Orthopedic surgery
- Plastic surgery
- Otorhinolaryngologic surgery
- General surgery
- Urologic procedure

**Non-surgical patients* (N=34)**

- Upper extremity pain
- Lower extremity pain
- Axial pain
- Multiple, concurrent pain conditions
- Orofacial pain

**Not inclusive* of all procedures and pain types in the study

# SUMMARY OF THE VX-548 PIVOTAL PROGRAM RESULTS IN ACUTE PAIN

# TREATMENT WITH VX-548 SHOWED STATISTICALLY SIGNIFICANT PAIN RELIEF COMPARED TO PLACEBO IN BOTH RANDOMIZED CONTROLLED TRIALS

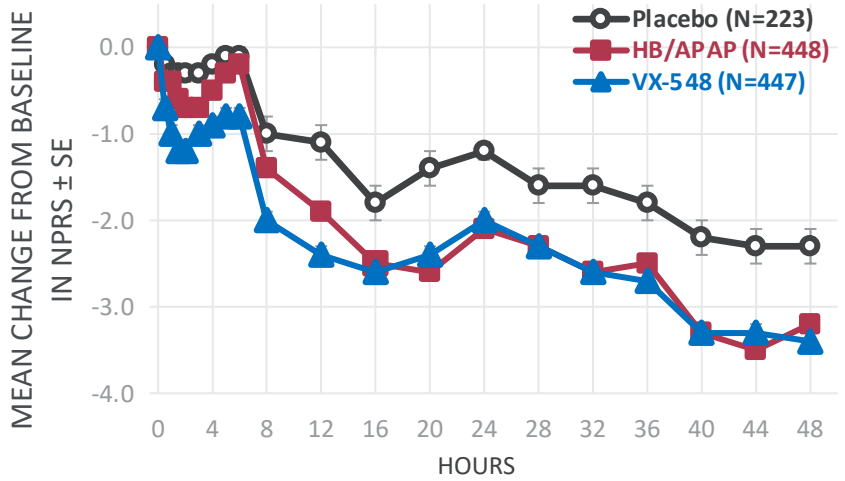
## Primary endpoint: SPID48 VX-548 vs. placebo

| | 548-105 ABDOMINOPLASTY | | 548-104 BUNIONECTOMY | |
|---|---|---|---|---|
| | PLACEBO<br>N=223 | VX-548<br>100 mg, 50 mg q12h<br>N=447 | PLACEBO<br>N=216 | VX-548<br>100 mg, 50 mg q12h<br>N=426 |
| SPID48 LS mean (SE) | 70.1<br>(6.1) | 118.4<br>(4.3) | 70.6<br>(6.3) | 99.9<br>(4.5) |
| SPID48 LS mean difference from placebo | | **48.4** | | **29.3** |
| 95% CI | | (33.6, 63.1) | | (14.0, 44.6) |
| *P* value vs. placebo | | <0.0001 | | 0.0002 |

SPID48 = time-weighted sum of the pain intensity difference (SPID) from 0 to 48 hours; LS = least squares; SE = standard error; CI = confidence interval; q12h = every 12 hours

# REDUCTION IN PAIN WAS RAPID, SUSTAINED AND CLINICALLY MEANINGFUL IN BOTH TRIALS

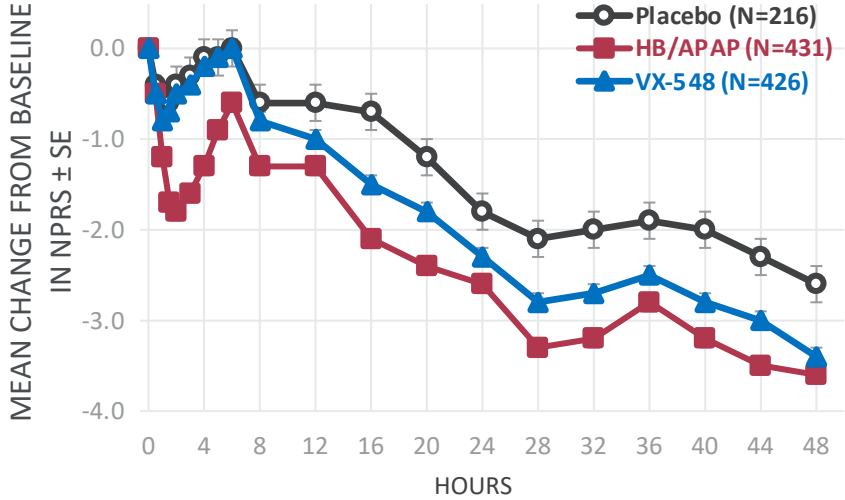
## 548-105 ABDOMINOPLASTY




## 548-105 ABDOMINOPLASTY

| | PLACEBO N=223 | HB/APAP 5 mg / 325 mg q6h N=448 | VX-548 100 mg, 50 mg q12h N=447 |
|---|---|---|---|
| Baseline NPRS, mean | 7.5 | 7.4 | 7.3 |
| Change from baseline in NPRS, mean | -2.3 | -3.2 | **-3.4** |
| % reduction from baseline in mean NPRS | 31% | 43% | **47%** |

## 548-104 BUNIONECTOMY




## 548-104 BUNIONECTOMY

| | PLACEBO N=216 | HB/APAP 5 mg / 325 mg q6h N=431 | VX-548 100 mg, 50 mg q12h N=426 |
|---|---|---|---|
| Baseline NPRS, mean | 6.8 | 6.8 | 6.7 |
| Change from baseline in NPRS, mean | -2.6 | -3.6 | **-3.4** |
| % reduction from baseline in mean NPRS | 38% | 53% | **51%** |

NPRS = numeric pain rating scale; SE = standard error; HB/APAP = hydrocodone bitartrate/ acetaminophen; q6h = every 6 hours; q12h = every 12 hours

# VX-548 EFFICACY IS COMPELLING AND CONSISTENT WITH OPIOID STUDIES FOLLOWING BUNIONECTOMY AND ABDOMINOPLASTY SURGERY

| Program | Study Population | Sample size (N treated) | Treatment group | SPID48 | |
|---|---|---|---|---|---|
| | | | | Placebo mean | Mean difference from placebo |
| VX-548 Phase 2 Program | ABD | ~76 per group | Placebo | 72.7 | |
| | | | HB/APAP 5/325 mg q6h | -- | 12.5 |
| | | | VX-548 100 mg, 50 mg q12h | -- | 37.8 |
| | BUN | ~60 per group | Placebo | 101.0 | -- |
| | | | HB/APAP 5/325 mg q6h | -- | 14.7 |
| | | | VX-548 100 mg, 50 mg q12h | -- | 36.8 |
| VX-548 Phase 3 Program | ABD | 223 for placebo<br>~447 per group for HB/APAP and VX-548 | Placebo | 70.1 | -- |
| | | | HB/APAP 5/325 mg q6h | -- | 41.7 |
| | | | VX-548 100 mg, 50 mg q12h | -- | 48.4 |
| | BUN | 216 for placebo<br>~428 per group for HB/APAP and VX-548 | Placebo | 70.6 | |
| | | | HB/APAP 5/325 mg q6h | -- | 49.5 |
| | | | VX-548 100 mg, 50 mg q12h | -- | 29.3 |
| IV Tramadol Phase 3 Program | ABD[1,3] | 136 for placebo<br>141 for IV tramadol<br>93 for IV morphine | Placebo | 121.1 | -- |
| | | | IV tramadol 50 mg q2h x3 doses; then q4h | -- | 59.7 |
| | | | IV morphine 4 mg q2h x3 doses; then q4h | -- | 57.5 |
| | BUN[2,3] | ~136 per group | Placebo | 97.8 | -- |
| | | | IV tramadol 25 mg q2h x3 doses; then q4h | -- | 13.1 |
| | | | IV tramadol 50 mg q2h x3 doses; then q4h | -- | 25.0 |
| IV Oliceridine Phase 3 Program | ABD*[4] | ~80 per group | Placebo | 149.6 | -- |
| | | | Oliceridine 0.1 mg[#] | -- | 4.0 |
| | | | Oliceridine 0.35 mg[#] | -- | 29.8 |
| | | | Oliceridine 0.5 mg[#] | -- | 38.4 |
| | | | IV Morphine[†] | -- | 56.2 |
| | BUN[4] | ~78 per group | Placebo | 85.0 | -- |
| | | | Oliceridine 0.1 mg[#] | -- | 46.4 |
| | | | Oliceridine 0.35 mg[#] | -- | 53.1 |
| | | | Oliceridine 0.5 mg[#] | -- | 78.7 |
| | | | IV Morphine[†] | -- | 107.6 |

ABD=Abdominoplasty; BUN=Bunionectomy

IV tramadol was not approved in the U.S.; approved in multiple counties ex-U.S. inclusive of EU and others. SPID48 values for the IV tramadol studies were converted by multiplying the reported values by -1 to allow for comparability with results from other studies. IV oliceridine was approved in the U.S.

*SPID48 values for the oliceridine ABD study were estimated by multiplying the reported SPID24 values by 2 to allow for comparability with results from other studies.

[#]IV PCA: clinician loading dose, then 1 patient dose q6min prn + 1 clinician bolus q1hr prn.

[†]Loading dose of 4 mg, demand dose of 1 mg, lockout interval of 6 minutes and supplementary dose 2 mg q1h prn.


[1]Minkowitz, et al., Drugs in R&D (2020) 20:225-236

[2]Singla, et al., Pain Ther (2020) 9:545-562

[3]AADPAC and DsARM Meeting FDA Briefing document for NDA 213231, Feb 2022

[4]AADPAC Meeting FDA Briefing document for NDA 210730, Oct 2018

# VX-548 WAS SAFE AND WELL TOLERATED IN THESE TRIALS WITH >2,400 PATIENTS WITH MODERATE TO SEVERE ACUTE PAIN

Results support broad label in moderate to severe acute pain

**VX-548**

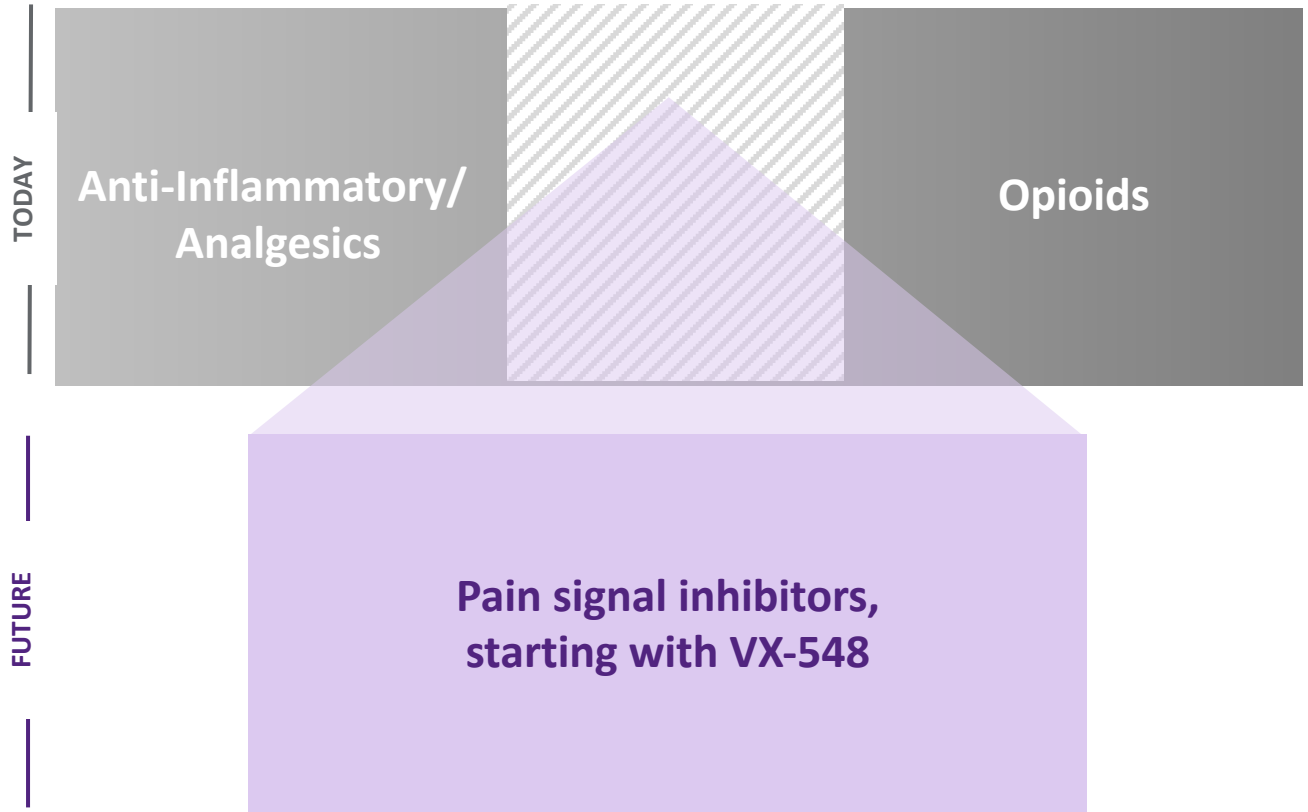
- Across all three studies, the majority of AEs with VX-548 were mild or moderate in severity
- Across all three studies, there were no SAEs related to VX-548
- In general, AEs in the two RCTs were consistent with the post-surgical setting
- In the two RCTs, the incidence of AEs in VX-548 arms was lower than placebo

RCT = randomized controlled trial

# RESULTS SUPPORT BROAD USE OF VX-548 IN MODERATE TO SEVERE ACUTE PAIN

Acute pain is a multi-billion dollar market today, with significant unmet need

- **80M patients** are prescribed a medicine for moderate to severe acute pain every year in the U.S.
- **Multi-billion dollar market** today despite being virtually entirely generics
- **Existing treatment options have limitations** on efficacy, side effects and addiction potential
- A novel class of **non-opioid pain signal inhibitors, starting with VX-548,** could **transform the treatment of acute pain**



# VERTEX IS COMMITTED TO TRANSFORMING THE TREATMENT OF PAIN

## SERIAL INNOVATION, BROAD/DEEP PIPELINE FOR LEADERSHIP IN MULTIPLE PAIN STATES GIVEN HIGH UNMET NEED

| | FORMULATION | RESEARCH | PHASE 1 | PHASE 2 | PHASE 3 | APPROVED |
|---|---|---|---|---|---|---|
| **VX-548 $Na_V1.8$ inhibitor* - Acute pain** | Oral | | | | | |
| **VX-548 $Na_V1.8$ inhibitor - DPN** | Oral | | | | | |
| **VX-548 $Na_V1.8$ inhibitor - LSR** | Oral | | | | | |
| **VX-993 $Na_V1.8$ inhibitor** | Oral | | | | | |
| **VX-973 $Na_V1.8$ inhibitor** | Oral | | | | | |
| **VX-993 $Na_V1.8$ inhibitor** | IV | | | | | |
| **Additional $Na_V1.8$ inhibitors** | Oral and IV | | | | | |
| **$Na_V1.7$ inhibitors** | Oral | | | | | |

Acute Pain

Peripheral Neuropathic Pain (PNP)

DPN: diabetic peripheral neuropathy; LSR: lumbosacral radiculopathy; IV: intravenous

# POSITIVE RESULTS IN THREE PHASE 3 TRIALS OF VX-548 IN ACUTE PAIN ARE THE CORNERSTONE OF VERTEX'S GOAL TO TRANSFORM THE TREATMENT OF PAIN

- VX-548 is a highly selective pain signal inhibitor
  - First novel mechanism for acute pain in over 20 years
- Positive results in two RCTs and SASE study demonstrate compelling combination of safety and efficacy
- Pivotal program results support broad use of VX-548 across multiple types of acute pain and different settings
- On track for mid-2024 NDA submission in the U.S., targeting broad moderate to severe acute pain indication
  - Fast Track and Breakthrough Therapy designations
- Pre-launch activities underway

RCT = randomized controlled trial; SASE = single arm safety and effectiveness study

VERTEX

THE SCIENCE *of* POSSIBILITY

# VERTEX PHARMACEUTICALS

JANUARY 30, 2024