SPRAVATO® (esketamine)
Oregon Pharmacy and Therapeutics (P&T) Committee Meeting - Written Medicaid Testimony - April 2025

INTRODUCTION/ PRODUCT DESCRIPTION

SPRAVATO is a non-competitive N-methyl D-aspartate (NMDA) receptor antagonist indicated for the treatment of:

- Treatment-resistant depression (TRD) in adults, as monotherapy or in conjunction with an oral antidepressant[1] AND
- Depressive symptoms in adults with major depressive disorder (MDD) with acute suicidal ideation or behavior in conjunction with an oral antidepressant.[1]

Please note Limitations of Use Including:[1]

- The effectiveness of SPRAVATO in preventing suicide or in reducing suicidal ideation or behavior has not been demonstrated. Use of SPRAVATO does not preclude the need for hospitalization if clinically warranted, even if patients experience improvement after an initial dose of SPRAVATO.
- SPRAVATO is not approved as an anesthetic agent. The safety and effectiveness of SPRAVATO as an anesthetic agent have not been established.

SPRAVATO has a boxed warning for sedation, dissociation, respiratory depression, abuse and misuse, and suicidal thoughts and behaviors.[1]

SPRAVATO is a Schedule III (CIII) controlled substance under the Controlled Substances Act. Due to the risks of serious adverse outcomes from sedation, dissociation, respiratory depression, abuse and misuse, SPRAVATO is available only through a restricted program called SPRAVATO Risk Evaluation and Mitigation Strategies (REMS). Further information is available at SPRAVATOrems.com.[1]

The most common adverse events in patients treated with SPRAVATO monotherapy (≥5% and at least twice that of placebo nasal spray) observed in TRD include: dissociation, dizziness, nausea, sedation, vertigo, hypoesthesia, anxiety, lethargy, blood pressure increased, vomiting, feeling drunk, and headache.[1]

BACKGROUND

TRD and MDSI are two clinically distinct populations, although overlap may occur.[2] Although there is no consensus on the definition of TRD, TRD is commonly defined as a failure to achieve response or remission after ≥2 treatment attempts of adequate dose and duration in the current depressive episode.[3] The Sequenced Treatment Alternatives to Relieve Depression (STAR*D) trial demonstrated that one-third of patients with MDD do not achieve remission. The study found that only 37% of patients responded to initial treatment, and the proportion of patients achieving remission dropped to 31% with the second treatment trial and 14% with the third treatment trial.[4]

The PI for SPRAVATO nasal spray does not restrict treatment to a specific REMS certified treatment setting (i.e. inpatient or outpatient). Current guidelines including the American Psychiatric Association's guidelines on MDD and the Zero Suicide Initiative recommend that the psychiatrist should determine the least restrictive setting for treatment that will not only address the patient's safety, but also promote improvement in the patient's condition.[5,6] Use of SPRAVATO does not preclude the need for hospitalization if clinically warranted, even if patients experience improvement after an initial dose of SPRAVATO.

The FDA issued an alert in February 2022 and October 2023, due to increased safety reports following the use of compounded ketamine nasal spray and compounded oral products, respectively.[7,8] Unlike esketamine, racemic ketamine has been associated with brain lesions in animal models.[7] Additionally, ketamine is not FDA-approved for the treatment of any psychiatric disorder. The FDA recommends healthcare professionals be aware of the potential risks associated with compounded ketamine products.[7,8]

CLINICAL DATA OVERVIEW

The efficacy and safety of SPRAVATO monotherapy use in TRD in adults was evaluated in a phase 4 study and long-term open label safety study.[9-11]

Janik et al (2024) NCT04599855[9,10]

NCT04599855 was a multicenter, phase 4, double-blind, randomized, placebo-controlled study, with screening (up to 7 weeks), double-blind treatment (4 weeks), open-label treatment/observation (up to 3 months), and follow-up (1 week) phases. In the double-blind phase, patients were randomized 2:1:1 to receive placebo nasal spray, SPRAVATO 56 mg, or SPRAVATO 84 mg. In the open-label treatment/observation phase, patients received SPRAVATO 56/84 mg with or without standard-of-care. Of the 477 patients with TRD randomized, 378 met the non-response criteria* and received study medication and were included in the full analysis set (placebo, n=197; SPRAVATO 56 mg, n=86; SPRAVATO 84 mg, n=95). The primary endpoint of change in MADRS total score from baseline to day 28 showed statistically significant and clinically meaningful improvement with both SPRAVATO doses (56 mg and 84 mg) compared to placebo (P<0.001). The key secondary endpoint of change in MADRS total score from baseline to day 2 (~24 hours after first dose) showed greater improvement in the SPRAVATO groups compared to placebo (P=0.004 for SPRAVATO 56 mg and P=0.006 SPRAVATO 84 mg). Higher response rates (≥50% reduction in MADRS total scores from baseline) were seen in the SPRAVATO 56 mg (30.5%) and SPRAVATO 84 mg (29.2%) groups compared to placebo (15.1%) at day 28. Remission rates based on MADRS total scores of ≤10 were higher in both SPRAVATO groups compared to placebo at all double-blind timepoints. Remission rates for SPRAVATO 56 mg, SPRAVATO 84 mg, and placebo groups were 14.6%, 21.3%, and 6.5%, respectively on day 28. Overall, rates of patients who reported ≥1 TEAE during the double-blind phase were as follows: 72.4% in SPRAVATO 56 mg and 75.2% in SPRAVATO 84 mg, and 49.2% in PBO. During the open-label phase, all patients received SPRAVATO regardless of their previous double-blind treatment. TEAE rates were reported based on their previous double-blind treatment: 64.6% in SPRAVATO 56 mg/SPRAVATO, 63.8% in SPRAVATO 84 mg/SPRAVATO, and 73.4% in PBO/SPRAVATO. The most common (≥10%) TEAEs during the

double-blind and open-label phase were nausea, dissociation, dizziness, and headache. The majority of TEAEs were transient. No deaths were reported in either the double-blind or open-label phase.

*Non-response criteria (blinded to study sites): MADRS, total score of ≥ 28 at screening week 1, week 2 and day 1 (pre-randomization) and ≤ 25% improvement in the MADRS total score from screening week 1 to day 1 (pre-randomization)

Fu et al (2022) POST-HOC ANALYSIS of SUSTAIN-3[11]

SUSTAIN-3, a phase 3, open-label, single-arm extension study evaluated the long-term safety and efficacy of flexibly-dosed SPRAVATO in adults with TRD. A post-hoc analysis of the interim report of the SUSTAIN-3 study characterized the safety and efficacy of SPRAVATO monotherapy in TRD. The study included 50 patients aged 18-74 years who participated in the phase 3 open-label safety extension study. Of those 50 patients, 21 patients never received oral antidepressants treatment during SUSTAIN-3 and 29 patients who discontinued oral antidepressants and continued SPRAVATO monotherapy ≥3 months during SUSTAIN-3. Severity of depression remained stable from optimization/maintenance (OP/M) baseline to endpoint. Remission rates, measured by MADRS (total score ≤ 12) and PHQ-9 (total score<5), were similar between OP/M baseline and endpoint. The proportion of patients in remission (MADRS score ≤12) was 50.0% (25 of 50 patients) at OP/M baseline and 53.1% (26 of 49 patients) at the OP/M endpoint. The proportion of patients in remission (according to PHQ-9 score <5) was 30.0% (15 of 50 patients) at OP/M baseline and 38.8% (19 of 49 patients) at the OP/M endpoint. The most common TEAEs (≥20%) and corresponding rates from the overall SUSTAIN-3 study population were similar, and included headache, dizziness, nausea, anxiety, diarrhea, and upper respiratory tract infection.

Ahmed et al (2024) 5-year REMS Data[12]

The 5-year REMS database analysis (March 5, 2019, to January 5, 2024) included 58,483 patients who had ≥1 SPRAVATO treatment session(s). The mean age of the patients was 43.4 years, with 61.1% being female. The mean (range) number of treatment sessions per patient was 25.4 (1-420), with 75.1% receiving ≥9 sessions and 60.3% receiving ≥13 sessions. Patients transitioned from SPRAVATO 56 mg to 84 mg over time, with ≥80% receiving 84 mg by session 6. Patients aged >75 years received SPRAVATO 84 mg at the lowest frequency.

AEs of special interest (ie, sedation, dissociation, increased BP) were observed in 76.8% of patients, and in 51.4% of treatment sessions. Sedation, dissociation, and increased BP were recorded in 61.9%, 65.7%, and 11.7% of patients, respectively, and in 34.7%, 41.0%, and 0.9% of overall treatment sessions, respectively. The incidence rates of sedation and dissociation reduced during induction from session 1-8 and remained relatively consistent during maintenance. The incidence rate of increased BP reduced from 1.6% to <1% during induction from session 1-8. The incidence of AEs of special interest was similar between men and women (76.9% vs 76.8%, respectively), with men reporting more increased BP events than women (13.4% vs 10.6%, respectively). The incidence of sedation and dissociation were similar amongst patients of all age groups; however, the incidence of increased BP events was higher in patients aged ≥25 years vs those aged <25 years (25-55 years, 11.7%; >55 years, 12.9%; <25 years, 6.8%).

SAEs were observed in 1.6% of patients, and in <0.1% of treatment sessions. The incidence rate of SAEs reduced from 0.26% to below 0.1% during induction from session 1-8*. The incidence rate of SAEs did not vary with sex. Patients aged <25 years experienced fewer SAEs (1.1%) vs those aged 25-55 years (1.5%) and >55 years (1.9%). Of the SAEs reported (N=2096), the most common were vomiting (n [%], 157 [7.5%]), increased BP (142 [6.8%]), nausea (141 [6.7%]), dizziness (103 [4.9%]), unevaluable events (85 [4.1%]), and dissociation (83 [4.0%]).

*This trend was noted even though >80% of patients received a lower initial dosage of 56 mg.

CONCLUSION

In summary, SPRAVATO, a non-competitive NMDA receptor antagonist, is indicated for the treatment of TRD as monotherapy or in conjunction with an oral antidepressant, and MDSI in conjunction with an oral antidepressant. SPRAVATO has a boxed warning for sedation, dissociation, respiratory depression, abuse and misuse, and suicidal thoughts and behaviors. Due to the risk of these serious outcomes, SPRAVATO is only available through a restricted SPRAVATO REMS program. Please see the full Prescribing Information for complete information.[1]

SPRAVATO monotherapy has demonstrated efficacy and safety in the treatment of TRD when compared to placebo. In the multicenter phase 4 study (NCT04599855), SPRAVATO achieved statistically significant and clinically meaningful improvement in MADRS total score from baseline to day 28 and day 2 compared to placebo.[9,10] Post-hoc analysis of the long term open-label safety study show that the safety profile of SPRAVATO monotherapy use is consistent with the overall study and that depressive symptoms remained stable.[11]

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Thank you for the opportunity to submit a public testimony regarding *JOURNAVX™ (suzetrigine)*, a first in class, oral, $Na_V1.8$ sodium channel blocker, indicated for the treatment of moderate-to-severe acute pain in adults.[1,2]

The contraindication and complete list of Warnings, Precautions, and Adverse Reactions associated with JOURNAVX has been previously shared and can be found in the JOURNAVX prescribing information.[1]

Disease State: Acute Pain

Acute pain is a condition that is characterized by sudden onset and is often caused by injury, surgery, or trauma, lasting less than 3 months and significantly disrupting daily activities.[3-5] It is estimated that ~82.9 million adults suffer from acute pain requiring management with pain medication.[6,7] Despite current treatments, there remains a significant unmet need for patients in the United States (US).

Acute Pain Treatment Landscape & Unmet Need

The current treatment of acute pain generally consists of non-steroidal anti-inflammatory drugs (NSAIDs) and acetaminophen, which have limited efficacy in moderate-to-severe pain, and opioids, which are effective for moderate-to-severe pain, but have tolerability concerns and carry risk of addiction.[8,9] Until now, opioids were the only oral monotherapy indicated for initial treatment of moderate-to-severe acute pain.[8] While effective, they activate the brain reward system within the central nervous system, which can cause opioid misuse, addiction, and opioid use disorder (OUD).[8,10-12] OUD is a clinically diagnosed condition based on criteria including failure to control use or opioid use that results in an inability to fulfill work, school, or home obligations.[13]

The current treatment landscape for acute pain has led to the following important consequences:[14-18]

(1) Inadequately managed acute pain, which can have a significant negative impact on patient quality of life including sleep interruption, depression, immobility, inability to work as well as an increased risk of developing chronic pain;
(2) Tolerability challenges including opioid-related adverse events (ORADEs) that lead to increased morbidity and are associated with high healthcare costs; and
(3) The opioid epidemic, which continues to plague the US, with the prevalence of OUD estimated to be over 7 million people.

Opioid-related overdoses have increased nearly every year since 1999, with nearly 80,000 reported deaths in recent years[19-21] (of which ~17% directly involved prescription opioids[21]), and the epidemic costs the US economy upwards of $180 billion per year, of which nearly $60 billion is attributed to healthcare costs.[19]

In an analysis of opioid-naïve patients who received prescription opioids for management of acute pain in the US, the 1-, 2-, and 3-year incidence rates of OUD among acute pain patients with prescription opioids in the Medicaid population are 3.13%, 4.57%, and 5.68%.[22] These are much higher compared to commercial and Medicare populations which range from 0.11% to 0.44%. Among the Medicaid population, the 2023 associated per patient total all-cause healthcare costs for patients diagnosed with OUD were $16,006 in the first year after OUD diagnosis compared to $7,119 for one-year healthcare costs for patients without OUD.[22]

Opioid prescriptions for acute pain may also lead to new persistent opioid use (NPOU) and OUD.[10] NPOU occurs when an opioid-naïve patient receives a post-operative opioid prescription meant for short-term use but continues to fill additional opioid prescriptions for months after this initial exposure.[23]

A retrospective cohort study showed that patients receiving an opioid prescription within 7 days of a short-stay surgery have a 44% increased risk of long-term opioid use within 1-year.[24] Another study reported approximately 6% of opioid-naïve adults develop NPOU after undergoing surgery.[25] NPOU is not only a consequence of poorly-controlled perioperative pain, but further contributes to poor patient outcomes, including increased rates of mortality, OUD, serious falls or fall-related injuries, and respiratory complications.[26] Adults reporting prescription opioid misuse have also demonstrated a substantial humanistic impact such as significantly higher risk of suicidality.[27]

According to a Kaiser Family Foundation analysis, ~3% of all Medicaid beneficiaries have a diagnosis of OUD.[28] Furthermore, compared to commercially insured beneficiaries, previously opioid-naïve Medicaid beneficiaries are almost 3.8 times more likely to experience an overdose after being prescribed an opioid.[29] Beyond the impact of opioid use, inadequate pain management itself has consequences on healthcare resource utilization.[30]

Health Disparities

Racial and ethnic inequities in acute pain management, including barriers to opioid access, which lead to the undertreatment of pain in certain populations are another important area to consider.[31-33] Treatments that could improve the pain management of historically underserved populations and reduce the burden of the opioid epidemic which disproportionately affects Black/African Americans are important for improving patient care and reducing health disparities.[34]

JOURNAVX: Mechanism of Action & Lack of Addiction Potential

In contrast to opioids, *JOURNAVX* is a selective blocker of the $Na_V1.8$[1] and is not expected to interact with opioid receptors based on available data, including the mechanism of action, preclinical data, and clinical adverse event data.[35] By selectively inhibiting $Na_V1.8$ channels, *JOURNAVX* inhibits transmission of pain signals to the spinal cord and brain.[1] Since $Na_V1.8$ is selectively expressed in peripheral sensory neurons and there is no $Na_V1.8$ expression in the human brain, selective inhibitors of $Na_V1.8$ channels are not expected to have abuse or addictive potential due to this mechanism of action.[35]

JOURNAVX, indicated for the treatment of moderate-to-severe acute pain in adults, has a novel mechanism of action as a selective blocker of the $Na_V1.8$ voltage-gated sodium channel in peripheral sensory neurons.[1,35]

Safety & Efficacy

The efficacy of *JOURNAVX* in moderate-to-severe acute pain was evaluated in two Phase 3 randomized, double-blind, placebo- and active-controlled studies following full abdominoplasty and bunionectomy surgery.[1]

Participants were randomized to receive *JOURNAVX*, placebo, or hydrocodone bitartrate/acetaminophen (HB/APAP).[1] Both trials evaluated the efficacy of *JOURNAVX* over 48 hours in 1,118 adult patients (*JOURNAVX* n = 447, placebo n = 223, and HB/APAP n = 448) following a full abdominoplasty procedure and 1,073 adult patients (*JOURNAVX* n = 426, placebo n = 216, and HB/APAP n = 431) following bunionectomy.[36]

In clinical trials, pain is often assessed with the 11-point Numeric Pain Rating Scale (NPRS) ranging from 0 to 10, where scores of 4 to 6 and 7 to 10 represent moderate and severe pain, respectively.[37]

In both trials, participants administered *JOURNAVX* achieved superior relief of moderate-to-severe acute pain demonstrated by significant reductions in pain versus placebo.[1] The primary endpoint was time-weighted sum of the pain intensity difference (SPID) over 48 hours of treatment (SPID48) compared with placebo.[1] SPID is a validated regulatory endpoint used to evaluate pain treatments in clinical trials; it measures pain intensity (NPRS scores) over time where higher SPID values represent greater reduction in pain.[38] SPID48 can help evaluate how much pain relief a patient experiences, compared with their baseline pain level before starting the intervention, over a 48-hour period. *JOURNAVX* achieved significant pain reduction versus placebo in participants receiving full abdominoplasty and bunionectomy with a LS mean difference of 48.4 and 29.3 following each surgical procedure.[1] *JOURNAVX* was associated with a 47% reduction and a 51% reduction on the NPRS from baseline at 48 hours in participants receiving abdominoplasty and bunionectomy, respectively.[36]

The key secondary endpoint was intended to demonstrate *JOURNAVX* superiority compared with HB/APAP 5 mg/325 mg every 6 hours and was not met following full abdominoplasty or bunionectomy.[39]

The safety profile of *JOURNAVX* is primarily based on data from the pooling of both trials in 874 participants with moderate-to-severe acute pain that received at least one dose of *JOURNAVX*.[1] *JOURNAVX* was generally well-tolerated with low rates of discontinuation.[1,39] The proportion of participants who discontinued study drug prematurely due to adverse events (AEs) was 0.6% following *JOURNAVX*, 0.6% following HB/APAP and 0.2% following placebo.[1] The incidence of nausea or vomiting was lower for *JOURNAVX* versus HB/APAP (Full abdominoplasty: 20% vs 33%; Bunionectomy: 9% vs 16%).[1] Most AEs were mild to moderate and there were no serious adverse events related to *JOURNAVX*.[39]

A third Phase 3 study of single-arm, open-label use evaluated safety of *JOURNAVX* in 256 participants with moderate-to-severe acute pain following a broad range of surgical procedures or non-surgical conditions.[1]

A total of 222 (87%) participants received *JOURNAVX* for post-surgical pain.[1] Orthopedic surgery was the most common, followed by plastic, otorhinolaryngologic, and general and urologic surgeries. A total of 34 (13%) participants received *JOURNAVX* for non-surgical pain (e.g., arthralgias, limb pain, and sprains/strains). The mean duration of treatment with *JOURNAVX* was 9.6 days.

The primary endpoint was safety and tolerability.[1] *JOURNAVX* was generally well-tolerated in a broad range of surgical procedures or nonsurgical pain conditions treated up to 14 days.[40] AEs were mostly mild or moderate, and there were no serious AEs related to *JOURNAVX*. The proportion of participants who discontinued study drug prematurely was 2% due to AEs and 1.6% due to lack of efficacy.[1] The safety profile of *JOURNAVX* was consistent with that observed in the full abdominoplasty and bunionectomy trials.

Budget Impact

The Vertex budget impact model results suggest that *JOURNAVX* will have a limited budget impact in the first two years on formulary given projected reductions in OUD/opioid abuse and AEs for patients with moderate-to-severe acute pain.[41] Avoidance of AEs and opioid-related events with *JOURNAVX* offsets almost half of the incremental drug treatment costs.

Utilization is expected in a small percentage of patients due to physician familiarity with current pain management options; limited awareness and physician experience with *JOURNAVX* at launch;

heterogeneity of the acute pain population, including multiple different procedures and conditions where acute pain treatment is used; the anticipated patient fulfillment rates for an acute therapy; and a small, focused commercial footprint.

JOURNAVX is the first in a new class of medications indicated for moderate-to-severe acute pain in adults to be approved in over 20 years.[42,43] We are excited about the potential that *JOURNAVX* offers to adults suffering from moderate-to-severe acute pain.

Thank you for your consideration of this testimony.

Vertex Pharmaceuticals, Inc.

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Aimee Adelmann
Patient Advocate
adelmann.aimee@gmail.com
May 23, 2025

To: Oregon Health Authority, osupharm.di@oregonstate.edu
Subject: Support for Senate Bill 598

My name is Aimee Adelmann, and I am writing to express my strong support for Senate Bill 598, which ensures equal utilization review standards for opioid and nonopioid medications prescribed for the same treatment.

As a patient living with a rare disease and as a kidney transplant recipient, I have personally experienced the challenges of managing pain following surgeries and medical procedures. Effective pain management is critical to maintaining quality of life, yet current disparities in utilization review policies too often create barriers to accessing safer, nonopioid treatment options.

SB 598 represents a vital step toward more patient-centered care. By leveling the playing field between opioid and nonopioid medications, this legislation removes unnecessary administrative burdens that limit treatment choices. It empowers patients and providers to make informed, individualized decisions—supporting both effective pain relief and the reduction of opioid dependency.

This is not merely a policy issue; it is a matter of compassionate and equitable healthcare. Patients recovering from surgery or living with chronic pain should not have to overcome additional obstacles to access the safest and most appropriate treatments.

I urge the Oregon Health Authority to support and advance SB 598, ensuring all Oregonians have fair access to comprehensive pain management options.

Thank you for your time and thoughtful consideration.

Sincerely,
Aimee Adelmann

answer2cancer.org

Answer2Cancer is a comprehensive, patient-centric effort created *by* cancer patients *for* cancer patients and their caregivers and families.

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May 23, 2025

Attention: Members of the P&T Committee - osupharm.di@oregonstate.edu.

In working with hundreds of cancer patients and their families in and around Oregon, we write to you in the interest of more efficient and effective pain management for these patients – as well as patients of so many other clinical indications who must conquer pain in their treatment and post-acute care pathways.

Consider my personal situation. In 2013 I was diagnosed with advanced colorectal cancer and endured grueling weeks and months of radiation, surgeries, multiple rounds of toxic chemotherapy and post-acute pain that plagued me for a decade afterward. My wonderful and caring oncologist prescribed to me opioids and at each turn, I declined them. To be honest, I was nervous at the possibility of inadvertent dependence and very hesitant with opioids' telltale repercussions of constipation and bowel blockage. Such was not a possibility I would consider.

The options for pain management (per my private and excellent health care coverage) were severely limited so I had to rely on medicines that really weren't the optimal solutions, along with a lot of over-the-counter temporary remedies.

I endured four separate ER visits and subsequent hospitalizations because the pain was untenable. My post-treatment pain then was episodic but intense and at times, intolerable. I later learned the treatments had caused chronic inflammation in my lower colon, which prohibited healing and created many changes to my working and personal life schedule when the flare ups came (often without warning), rendering me unable to normally function.

In considering the devastating effects of both opioid use impacts and addiction across our state, a non-addictive option such as Suzetrigine/Journavx may well have been an optimal non-addictive treatment for me on every level. And, considering the opioid crisis, why wouldn't a non-addictive solution be prioritized for moderate to acute pain?

Uncontrolled and unmanaged pain costs Oregon on many levels. Pain is a known elemental piece of ever-increasing health care costs around the world when it is not properly addressed. Acute pain is responsible for lost productivity, higher drug costs overall and higher incidence of health care utilization. The ripple effects are undeniable. The Oregon Pain Commission recently said pain prevention, assessment and treatment are plainly **inadequate**.

What's also inadequate and, frankly, shortsighted, is the proposed process of prescribing and approval for Oregon's Medicaid population that would require an FDA-approved medicine such as Suzetrigine/Journavx to only be prescribed after patients fail on NSAIDs and acetaminophen (for mild to moderate pain) and an opioid for acute pain. The best thing the OHA in this situation could do is take such medications off of a 48-hour prior authorization configuration.

Finally, making pain medications harder for patients to get DOES NOT serve anyone – when you start to understand that it is **actually more expensive** to commit patients and prescribers to onerous pre-auth protocols that take more of a clinician's time and resources.

So to elevate the important mission of greatly (and simply) **improving pain treatment options away from opioids**, please consider the benefit for pain patients in elevating therapies that are non-addictive, then, make them easier to get. This is very much a win for the P&T Committee, for OHA, a win for prescribers and most importantly, a win for Oregon patients.

Sincerely,

Dianne Danowski-Smith

Founder and Chief Survivorship Officer, Answer2Cancer, Inc.