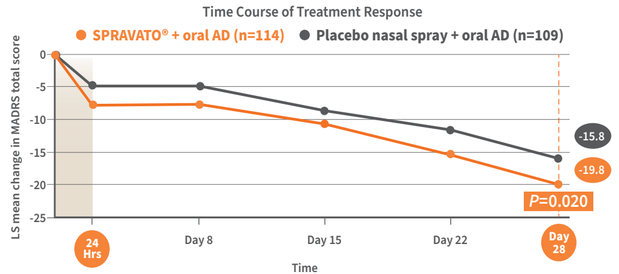
SPRAVATO® + oral AD demonstrated rapid and superior improvement in depressive symptoms compared to placebo + oral AD and offers your patients a consistent safety profile with minimal risk for sexual dysfunction [3-6]

Spravato® (esketamine) CIII
28 mg nasal spray

TRD Study 1 (Short-term)[3,4]



AD=antidepressant.
LS=least squares.
TRD=treatment-resistant depression.

Study Design[3,4]:

- Evaluated in a randomized, placebo-controlled, double-blind, short-term (4-week) study in adults with TRD (in current depressive episode and who had not responded to ≥2 different oral ADs adequately)
- Patients discontinued prior treatment and were randomized to receive twice-weekly doses of SPRAVATO® (flexible; 56 mg or 84 mg) plus a newly initiated oral AD or intranasal placebo plus newly initiated oral AD
- Primary endpoint was change from baseline in the Montgomery-Åsberg Depression Rating Scale (MADRS) total score at 4 weeks
- Patients across SPRAVATO® and placebo nasal spray groups had a median age of 47 years and were 62% female, 93% Caucasian, and 5% Black

Most of the treatment difference between SPRAVATO® and placebo was observed at 24 hours

Between 24 hours and Day 28, both SPRAVATO® and placebo groups continued to improve, and the difference between these 2 groups generally remained the same

Scan here to find out more about SPRAVATO® efficacy and safety

Most common adverse events (AEs)[3] (incidence ≥5% and at least twice that of placebo + oral AD)	SPRAVATO® + oral AD (N=346)	Placebo + oral AD (N=222)
Dissociation*	41%	9%
Dizziness*	29%	8%
Nausea	28%	9%
Sedation*	23%	9%
Vertigo*	23%	3%
Hypoesthesia*	18%	2%
Anxiety*	13%	6%
Lethargy*	11%	5%
Blood pressure increased*	10%	3%
Vomiting	9%	2%
Feeling drunk	5%	0.5%
Additional AEs in ≥2% of adults with TRD and at a greater rate than placebo (SPRAVATO® + oral AD vs placebo + oral AD)		
Headache* (20% vs 17%), Dysgeusia* (19% vs 14%), Insomnia (8% vs 7%), Diarrhea (7% vs 6%), Nasal discomfort* (7% vs 5%), Throat irritation (7% vs 4%), Dry mouth (5% vs 3%), Hyperhidrosis (4% vs 2%), Euphoric mood (4% vs 1%), Dysarthria* (4% vs 0%), Tremor (3% vs 1%), Oropharyngeal pain (3% vs 2%), Mental impairment (3% vs 1%), Constipation (3% vs 1%), Pollakiuria (3% vs 0.5%), Feeling abnormal (3% vs 0%), Tachycardia* (2% vs 0.5%)		

***The following terms were combined:**

Dissociation includes: delusional perception; depersonalization/derealization disorder; derealization; diplopia; dissociation; dysesthesia; feeling cold; feeling hot; feeling of body temperature change; hallucination; hallucination, auditory; hallucination, visual; hyperacusis; illusion; ocular discomfort; oral dysesthesia; paresthesia; paresthesia oral; pharyngeal paresthesia; photophobia; time perception altered; tinnitus; vision blurred; visual impairment
Dizziness includes: dizziness; dizziness exertional; dizziness postural; procedural dizziness
Sedation includes: altered state of consciousness; hypersomnia; sedation; somnolence
Vertigo includes: vertigo; vertigo positional
Hypoesthesia includes: hypoesthesia; hypoesthesia oral, hypoesthesia teeth, pharyngeal hypoesthesia
Anxiety includes: agitation; anticipatory anxiety; anxiety; fear; feeling jittery; irritability; nervousness; panic attack; tension
Lethargy includes: fatigue; lethargy
Blood pressure increased includes: blood pressure diastolic increased; blood pressure increased; blood pressure systolic increased; hypertension
Headache includes: headache; sinus headache
Dysgeusia includes: dysgeusia; hypogeusia
Nasal discomfort includes: nasal crusting; nasal discomfort; nasal dryness; nasal pruritus
Dysarthria includes: dysarthria; slow speech; speech disorder
Tachycardia includes: extrasystoles; heart rate increased; tachycardia

- **Most treatment-emergent adverse effects (TEAEs) (93.7%) occurred and resolved on the same day of dosing[5]**
  - In a 4-week study, the majority of dissociation (98.3%), blood pressure increase (86.4%), and sedation (83.3%) occurred and resolved on the same day of dosing[5]

You can have the confidence that SPRAVATO® demonstrated low discontinuation rates

4-week TRD short-term studies[1,2]

4.6% of patients taking SPRAVATO® discontinued treatment due to AEs

[1]Two short-term TRD studies in adults aged <65 years.

Sexual dysfunction was not observed in SPRAVATO® trials at a rate greater than 2%[6]

Important Safety Information (continued)

WARNINGS AND PRECAUTIONS (continued)

Sedation: (continued)
Closely monitor for sedation with concomitant use of SPRAVATO® with CNS depressants (e.g., benzodiazepines, opioids, alcohol).

Dissociation: The most common psychological effects of SPRAVATO® were dissociative or perceptual changes (including distortion of time, space and illusions), derealization and depersonalization (61% to 84% of SPRAVATO®-treated patients developed dissociative or perceptual changes). Given its potential to induce dissociative effects, carefully assess patients with psychosis before administering SPRAVATO®; treatment should be initiated only if the benefit outweighs the risk.

Please see additional Important Safety Information throughout this brochure, and full Prescribing Information, including Boxed WARNINGS, and Medication Guide for SPRAVATO®.

Important Safety Information (continued)

WARNINGS AND PRECAUTIONS (continued)

Dissociation: (continued)
Because of the risks of dissociation, patients must be monitored by a healthcare provider for at least 2 hours at each treatment session, followed by an assessment to determine when the patient is considered clinically stable and ready to leave the healthcare setting.

Respiratory Depression: In postmarketing experience, respiratory depression was observed with the use of SPRAVATO®. In addition, there were rare reports of respiratory arrest.

Because of the risks of respiratory depression, patients must be monitored for changes in respiratory status by a healthcare provider for at least 2 hours (including pulse oximetry) at each treatment session, followed by an assessment to determine when the patient is considered clinically stable and ready to leave the healthcare setting.

(continued on page 6)