HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use ISEMBYLD safely and effectively. See full prescribing information for ISEMBYLD.

ISEMBYLD™ (apitegromab-mstn) injection, for intravenous use
Initial U.S. Approval: 2026

----------INDICATIONS AND USAGE----------
ISEMBYLD is a recombinant monoclonal antibody targeting proforms of myostatin, indicated for the treatment of spinal muscular atrophy (SMA) in adults and pediatric patients 2 years of age and older who are currently receiving a survival motor neuron 2 (SMN2)-targeted treatment. (1)

----------DOSAGE AND ADMINISTRATION----------
- The recommended dosage of ISEMBYLD is 10 mg/kg administered once every 4 weeks as an intravenous infusion over approximately 60 minutes to 120 minutes at an infusion rate no greater than 150 mL/hour. (2.1, 2.4)
- ISEMBYLD must be diluted in 0.9% Sodium Chloride Injection prior to administration. (2.3)
- See Full Prescribing Information for important preparation and administration instructions. (2.3, 2.4)

----------DOSAGE FORMS AND STRENGTHS----------
Injection: 150 mg/3 mL (50 mg/mL) solution in a single-dose vial. (3)

----------CONTRAINDICATIONS----------
None. (4)

----------WARNINGS AND PRECAUTIONS----------
Fractures: Serious fracture events have occurred in patients treated with ISEMBYLD. Use with caution in patients with a history of low bone density or multiple fractures. In patients who experience fractures, weigh the risks and benefits of continuing ISEMBYLD. (5.1)

----------ADVERSE REACTIONS----------
Most common adverse reactions in SMA (incidence greater than or equal to 20% of patients treated with ISEMBYLD and more frequent than placebo) were upper respiratory tract infections, vomiting, cough, other viral infections, headache, gastroenteritis, pharyngitis, and hypersensitivity. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Scholar Rock, Inc. at 1-855-MED-SRRK (1-855-633-7775) or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

----------USE IN SPECIFIC POPULATIONS----------
- Pregnancy: Based on animal data, may cause fetal harm. (8.1)
- Females and Males of Reproductive Potential: Based on animal data, may affect reproductive function. (8.3)

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

Revised: 9/2026

FULL PRESCRIBING INFORMATION: CONTENTS*

*** Sections or subsections omitted from the full prescribing information are not listed**.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

ISEMBYLD is indicated for the treatment of spinal muscular atrophy (SMA) in adults and pediatric patients 2 years of age and older who are currently receiving a survival motor neuron 2 (SMN2)-targeted treatment.

2 DOSAGE AND ADMINISTRATION

2.1 Recommended Dosage

The recommended dosage of ISEMBYLD is 10 mg/kg administered once every 4 weeks as an intravenous infusion over approximately 60 minutes to 120 minutes at an infusion rate no greater than 150 mL/hour.

ISEMBYLD must be diluted prior to administration *[see Dosage and Administration (2.3)]*.

Doses of ISEMBYLD of 20 mg/kg administered once every 4 weeks were also assessed in Study 1; however, this dosage is not recommended as it did not demonstrate additional efficacy *[see Clinical Studies (14)]*.

2.2 Recommendations Regarding Missed Dose

If a planned dose is missed, it is recommended to administer ISEMBYLD as soon as possible and then restart the dosing schedule 4 weeks after the missed dose is administered *[see Dosage and Administration (2.1)]*.

Alternatively, if a planned dose is missed, dosing may be resumed on the next scheduled dose to maintain the original dosing schedule.

2.3 Preparation Instructions

ISEMBYLD must be diluted in 0.9% Sodium Chloride Injection to a final concentration of 5 mg/mL prior to intravenous infusion. The diluted solution for infusion must be prepared by a healthcare professional using aseptic technique as follows:

1. Calculate the required dose (mg) of ISEMBYLD to be administered based on the patient's weight and on the recommended dosage of 10 mg/kg. Determine the volume (mL) of ISEMBYLD needed and the correct number of vials to supply the calculated dose.
2. Remove ISEMBYLD vials from the refrigerator and allow vials to warm to room temperature while remaining in the carton until time of use. Do not use external heat sources to warm ISEMBYLD vials because heat may damage the product. Do not shake.
3. Visually inspect each vial of ISEMBYLD. ISEMBYLD is a clear to moderately opalescent, colorless to slightly yellow solution that is free from visible particulates. Do not use if the solution in the vial is discolored or particulate matter is present.
4. Withdraw the required volume of ISEMBYLD from each vial using a sterile syringe and transfer to an infusion bag that is di(2-ethylhexyl)phthalate (DEHP)-free.
5. Dilute ISEMBYLD to a final concentration of 5 mg/mL by adding the appropriate amount of 0.9% Sodium Chloride Injection to the infusion bag.
6. Gently invert the bag to mix the solution. Do not shake. Do not mix or dilute with other drugs.

7. Discard any unused ISEMBYLD remaining in the vial(s).
8. The diluted solution should be administered immediately after preparation. If not used immediately, store the infusion bag, protected from light, either at room temperature (20°C to 25°C [68°F to 77°F]) or in a refrigerator at 2°C to 8°C (36°F to 46°F) for up to 4 hours (including preparation and infusion time). Do not freeze.

2.4 Administration Instructions

1. If necessary, remove the diluted ISEMBYLD solution from the refrigerator and allow the diluted solution to warm to room temperature. Do not use external heat sources to warm ISEMBYLD diluted solution because heat may damage the product.
2. Visually inspect the diluted ISEMBYLD solution for particles or discoloration prior to administration *[see Dosage Forms and Strengths (3)]*. Do not use if it is discolored, opaque, or foreign particles are seen.
3. Use a dedicated line with an infusion set containing a 0.2 or 0.22 micron low protein binding polyethersulfone (PES) in-line infusion filter. Use infusion sets and lines that are di(2-ethylhexyl)phthalate (DEHP)-free.
4. Infuse the diluted solution of ISEMBYLD intravenously over approximately 60 minutes to 120 minutes at an infusion rate no greater than 150 mL/hour.
5. After completion of the infusion, flush the infusion line with 0.9% Sodium Chloride Injection to ensure that all the ISEMBYLD has been administered.

3 DOSAGE FORMS AND STRENGTHS

Injection: 150 mg/3 mL (50 mg/mL) apitegromab-mstn as a clear to moderately opalescent, colorless to slightly yellow solution in a single-dose vial.

4 CONTRAINDICATIONS

None.

5 WARNINGS AND PRECAUTIONS

5.1 Fractures

ISEMBYLD may increase the risk of fractures, including serious fractures *[see Adverse Reactions (6.1)]*. In Study 1 *[see Clinical Studies (14)]*, 5/53 (9%) of patients treated with ISEMBYLD 10 mg/kg and 3/53 (6%) of patients treated with ISEMBYLD 20 mg/kg (twice the recommended dosage) experienced fractures compared with one patient in the placebo group (2%) who had a fracture. Femur fractures occurred in three patients treated with ISEMBYLD in Study 1. No patients discontinued treatment due to fractures. In an ongoing open-label extension study in which patients received ISEMBYLD 20 mg/kg (twice the recommended dosage), fractures occurred in 22 patients (9%), including 5 serious events of femur fractures. Most patients with fractures had histories of low bone density previous fractures, or contractures. Some fracture events did not have a clear precipitating event (such as a fall).

Animal studies have also demonstrated adverse effects in bone *[see Nonclinical Toxicology (13.2)]*.

Use ISEMBYLD with caution in patients with a history of low bone density or multiple fractures. In patients who experience fractures, weigh the risks and benefits of continuing ISEMBYLD.

6 ADVERSE REACTIONS

The following clinically significant adverse reactions are described elsewhere in the labeling:

- Fractures *[see Warnings and Precautions (5.1)]*

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

The safety of ISEMBYLD for SMA was evaluated in a randomized, double-blind, and placebo-controlled study (Study 1) *[see Clinical Studies (14)]*. In Study 1, ISEMBYLD was evaluated in 128 patients with SMA (2 to 21 years at the start of the study), which included 53 patients 2 to 12 years of age [mean 7 years of age] who received the recommended dosage of ISEMBYLD (10 mg/kg once every 4 weeks) for a mean exposure of 49 weeks. Of those 53 patients, 43% were female, 66% were White, 11% were of Hispanic or Latino ethnicity, 4% were Asian, and 2% were Black or African-American. The adverse reaction information presented below is from the patients who received the recommended dosage of ISEMBYLD, unless otherwise noted.

The most common adverse reactions (reported in at least 20% of patients treated with ISEMBYLD and more frequently than in placebo) were upper respiratory tract infections, vomiting, cough, other viral infections, headache, gastroenteritis, pharyngitis, and hypersensitivity. Table 1 lists the common adverse reactions that occurred in at least 5% of patients treated with ISEMBYLD and at least 5% more frequently than placebo.

Table 1: Adverse Reactions Reported in ≥ 5% of Patients with SMA Treated with ISEMBYLD 10 mg/kg and ≥ 5% More Frequently than in Placebo (Study 1)

Adverse Reaction	ISEMBYLD 10 mg/kg (N = 53) %	Placebo (N = 50) %
Upper respiratory tract infections[1]	66	54
Vomiting	30	16
Cough	28	22
Other viral infections[2]	26	16
Headache	23	16
Gastroenteritis[3]	23	8
Pharyngitis[4]	21	14
Hypersensitivity[5]	21	16
Diarrhea	17	0
Injection site reactions[6]	13	0
Abdominal pain[7]	13	6
Arthralgia	13	4
Contusion	11	6
Fall	11	6
Fractures[8]	9	2
Fatigue[9]	9	2
Pain in extremity	9	4
Hematoma	6	0
Myalgia	6	0

[1] Includes nasopharyngitis, rhinovirus infection, sinusitis, viral upper respiratory tract infection, upper respiratory tract infection, nasal congestion, rhinorrhea, rhinitis.
[2] Includes metapneumovirus infection, parvovirus B19 infection, COVID-19, respiratory syncytial virus infection, respiratory syncytial virus bronchiolitis, influenza, parainfluenzae, adenovirus, respiratory tract infection viral, and viral infection.
[3] Includes other similar terms.
[4] Includes pharyngitis, pharyngitis streptococcal, oropharyngeal pain.
[5] Includes dermatitis acneiform, dermatitis atopic, eczema, flushing, rash, rash maculo-papular, urticaria
[6] Includes application site reaction, catheter site pain, infusion related reaction, infusion site bruising, infusion site pain, injection site bruising, injection site pain.
[7] Includes other similar terms.
[8] Includes foot fracture, clavicle fracture, femur fracture, tibia fracture, torus fracture.
[9] Includes fatigue, lethargy.

Acute Respiratory Failure

In Study 1, serious events of acute respiratory failure in the setting of lower respiratory tract infections occurred in two patients treated with ISEMBYLD at a dose of 10 mg/kg and in one patient that received placebo.

Pneumonia

In Study 1, serious adverse events of pneumonia occurred in three patients treated with ISEMBYLD at a dose of 10 mg/kg and in no patients that received placebo.

Laboratory Findings

Creatine Phosphokinase

In Study 1, CPK increases were seen more frequently in patients treated with ISEMBYLD 10 mg/kg (n=53) compared to placebo (n=50). By month 12, mean CPK levels increased by 91 U/L in patients treated with ISEMBYLD compared to 3 U/L in placebo. Increases in CPK were seen in 28% of patients treated with ISEMBYLD, compared to 12% in placebo; among these, 3 patients (6%) treated with ISEMBYLD had CPK elevations of greater than 2.5 times the upper limit of normal (ULN), compared to none in placebo. Similar patterns of elevations were seen in patients receiving ISEMBYLD who were over 12 years of age compared to those 2 to 12 years of age. One patient with elevated CPK at baseline who received ISEMBYLD 20 mg/kg (twice the recommended dosage) in the 13 to 21 age group had further CPK increases to greater than 10 times the ULN. Patients with CPK elevations in Study 1 have generally been asymptomatic.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

There are no adequate data on the developmental risk associated with the use of ISEMBYLD in pregnant women. Monoclonal antibodies, such as apitegromab-mstn, are known to cross the placental barrier with a higher likelihood of fetal exposure with administration during the third trimester; therefore, apitegromab-mstn may be transported from the mother to the fetus across the placenta during the pregnancy. When apitegromab-mstn was administered by IV infusion to rats throughout pregnancy and lactation, adverse effects on offspring reproductive and neurobehavioral function were observed at clinically-relevant maternal apitegromab-mstn exposures *[see Animal Data]*.

In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively. The background risk of major birth defects and miscarriage for the indicated population is unknown.

Data

Animal Data

In a study in which pregnant rats were administered apitegromab-mstn (0, 30, 100, or 300 mg/kg) by intravenous injection once-weekly throughout organogenesis (gestation days 6 to 17), no adverse effects on embryofetal development were observed. The no-effect dose for adverse effects on embryofetal development (300 mg/kg) was associated with maternal apitegromab-mstn exposures (AUC) approximately 2.5 times that in humans at the maximum recommended human dose (MRHD) of 10 mg/kg.

Once-weekly intravenous administration of apitegromab-mstn (0, 30, 100, or 300 mg/kg) to rats throughout pregnancy and lactation, resulted in delayed sexual maturation and altered neurobehavioral function (increased auditory startle response) in offspring of both sexes at all doses and impaired reproductive function in male offspring at the highest dose. A no-effect dose for adverse effects on pre- and postnatal development was not identified. The lowest dose tested (30 mg/kg) was associated with maternal apitegromab-mstn exposures (AUC) lower than that in humans at the MRHD.

8.2 Lactation

Risk Summary

There are no data on the presence of apitegromab-mstn in human milk, the effects on the breastfed infant, or the effects of the drug on milk production. Maternal IgG is known to be present in human milk, and the potential for absorption of ISEMBYLD to lead to inhibition of myostatin activation in the breastfed infant is unknown. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for ISEMBYLD, and any potential adverse effects on the breastfed infant from ISEMBYLD, or from the underlying maternal condition.

8.3 Females and Males of Reproductive Potential

Animal data suggest adverse effects of apitegromab-mstn on male and/or female reproductive function following exposure during postnatal development or in adulthood *[see Use in Specific Populations (8.4) and Nonclinical Toxicology (13.1)]*.

8.4 Pediatric Use

The safety and effectiveness of ISEMBYLD for the treatment of spinal muscular atrophy have been established in pediatric patients 2 years of age and older. Use of ISEMBYLD for this indication is supported by evidence from an adequate and well-controlled study in pediatric patients 2 to 12 years of age, latent myostatin levels in pediatric patients 2 years of age and older, and pharmacokinetic (PK) modeling comparing pediatric patients 2 to 12 years of age to pediatric patients 13 years of age and older *[see Adverse Reactions (6.1), Clinical Pharmacology (12.2, 12.3), and Clinical Studies (14)]*.

Safety and effectiveness in pediatric patients younger than 2 years of age have not been established.

Juvenile Animal Toxicity Data

Once-weekly intravenous administration of apitegromab-mstn (0, 30, 100, or 300 mg/kg) to juvenile rats from Postnatal Day (PND) 21 through PND 63 resulted in adverse effects on female reproductive function. When female rats exposed to apitegromab-mstn during the postnatal period were mated with naïve males in adulthood, corpora lutea were decreased, preimplantation

loss was increased, and numbers of implantation sites and live fetuses were decreased. A no-effect dose was not identified. The lowest effect dose (30 mg/kg) was associated with apitegromab-mstn exposures (AUC) lower than that in humans at the maximum recommended human dose (MRHD) of 10 mg/kg.

Once-weekly subcutaneous administration of apitegromab-mstn (0, 30, 100, or 275 mg/kg) to juvenile rats from PND 7 through PND 28 produced no adverse effects on the developmental endpoints assessed; however, reproductive function was not evaluated. The highest dose tested (275 mg/kg) was associated with apitegromab-mstn exposures (AUC) approximately 7 times that in humans at the MRHD.

8.5 Geriatric Use

Clinical studies of ISEMBYLD did not include patients 65 years of age and older to determine whether they respond differently from younger patients.

11 DESCRIPTION

Apitegromab-mstn, which targets proforms of myostatin, is a fully human IgG4 lambda monoclonal antibody produced by recombinant DNA technology in Chinese Hamster Ovary cells and has an approximate molecular weight of 147 kDa.

ISEMBYLD (apitegromab-mstn) injection is a sterile, preservative-free, clear to moderately opalescent, colorless to slightly yellow solution supplied in a single-dose glass vial for intravenous use.

Each 3 mL single-dose vial contains 150 mg apitegromab-mstn and histidine (4.44 mg), L-histidine hydrochloride monohydrate (6.57 mg), sodium chloride (22.80 mg), polysorbate 80 (0.6 mg), and Water for Injection, USP. Hydrochloric acid was added to adjust the pH. The pH is approximately 6.0.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

ISEMBYLD is a fully human monoclonal IgG4 antibody that binds to promyostatin and latent myostatin and inhibits the activation of myostatin, blocking myostatin signaling.

12.2 Pharmacodynamics

In Study 1, the increase in serum total latent myostatin levels are comparable across ISEMBYLD 10 mg/kg and 20 mg/kg (twice the recommended dosage) doses in patients with SMA 2 to 12 years of age, and the 20 mg/kg dose in patients with SMA 13 years of age and older.

12.3 Pharmacokinetics

The PK of apitegromab-mstn were characterized in healthy adult subjects and in patients with SMA using population pharmacokinetic modeling.

Pharmacokinetics of apitegromab-mstn were linear and dose-proportional in the range of 10 mg/kg to 20 mg/kg (twice the recommended dosage) in patients with SMA.

Following administration of ISEMBYLD once every 4 weeks in patients with SMA, approximately 2-fold accumulation of apitegromab-mstn exposures were observed, and exposures reached steady state by approximately 16-20 weeks.

Distribution

The apitegromab-mstn mean (coefficient of variation % [CV%]) steady state volume of distribution in patients with SMA (2 to 21 years of age) was estimated to be 2.16 L (48%).

Elimination

Apitegromab-mstn is expected to be degraded into small peptides and amino acids via catabolism in the same manner as endogenous IgGs.

The mean value (CV%) of clearance of apitegromab-mstn in patients with SMA (2 to 21 years of age) was estimated to be 0.055 L/day (50%). The mean value (CV%) of the terminal elimination half-life of apitegromab-mstn was estimated to be 31.2 days (32%).

Specific Populations

Pediatric Patients
The PK of apitegromab-mstn was characterized in pediatric patients 2 years of age and older using a population pharmacokinetic model. Following weight-based dosing of ISEMBYLD 10 mg/kg, model-predicted steady state exposures (C_{max}, C_{trough} and AUC) of apitegromab-mstn was comparable between patients 2 to 12 years of age and 13 to 21 years of age.

Male and Female Patients and Racial or Ethnic Groups
Based on the population PK analysis, sex, race, and ethnicity had no effect on apitegromab-mstn PK in patients with SMA.

Patients with Renal or Hepatic Impairment
No clinical studies were conducted to evaluate the PK of apitegromab-mstn in patients with renal or hepatic impairment. Apitegromab-mstn is degraded by proteolytic enzymes and is not expected to undergo renal elimination or metabolism by hepatic enzymes.

Drug Interaction Studies

An effect of apitegromab-mstn on the PK of co-administered medications is not expected. Based on the population PK analysis, SMN-modulating therapies (nusinersen and risdiplam) had no effect on apitegromab-mstn PK in patients with SMA.

12.6 Immunogenicity

The observed incidence of anti-drug antibodies is highly dependent on the sensitivity and specificity of the assay. Differences in the assay methods preclude meaningful comparisons of the incidence of anti-drug antibodies in the studies described below with the incidence of anti-drug antibodies in other studies, including those of apitegromab-mstn or of other apitegromab products.

In up to 52 weeks of treatment in Study 1, 1/128 (0.8%) of patients treated with ISEMBYLD tested positive for treatment-emergent anti-apitegromab-mstn antibodies at a single time point. No neutralizing antibodies were detected; however, because of the limited data regarding anti-apitegromab-mstn antibodies, the effect of these antibodies on the pharmacokinetics, pharmacodynamics, safety, and/or effectiveness of apitegromab products is unknown.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenesis

Carcinogenicity studies have not been conducted with apitegromab-mstn.

Mutagenesis

Genetic toxicology studies have not been conducted with apitegromab-mstn.

Impairment of Fertility

Once-weekly intravenous injection of apitegromab-mstn (0, 30, 100, or 300 mg/kg) to rats prior to and during mating and continuing in females to gestation day 6 resulted in decreased sperm concentrations, estrous cycle disruption, decreased male and/or female mating and fertility indices, and increased postimplantation loss at all doses. A no-effect dose for adverse effects on fertility and early embryonic development was not identified. The lowest dose tested (30 mg/kg) was associated with apitegromab-mstn exposures (AUC) lower than that in humans at the MRHD.

13.2 Animal Toxicology

Adverse effects on bone were observed in toxicology studies conducted in rats. In a study in which apitegromab-mstn (0, 10, 30, 100, or 300 mg/kg) was administered weekly by intravenous injection for 12 weeks, fissure at the femoral head physis was observed at all doses at the end of the dosing and recovery periods. The fissure was associated with partial or complete absence of the epiphysis and with degenerative (resorption) and reactive (fibrosis, woven bone, hyperplastic osteoclasts) changes at the femoral neck and proximal metaphysis. Qualitative findings of partial or complete missing femoral head epiphysis were observed in computed tomography images of apitegromab-mstn-exposed animals. Weekly intravenous administration of apitegromab-mstn (0, 30, 100, or 300 mg/kg) to rats for 26 weeks resulted in a dose-related increase in the incidence and severity of adverse changes in the femoral head/neck (femoral head loss, thinning, fracture, fragmentation of the femoral neck) observed by in vivo radiography at the end of the dosing and recovery periods.

A no-effect dose for bone effects was not identified. The lowest effect doses for adverse effects on bone in 12- and 26-week studies in rats (10 and 30 mg/kg, respectively) were associated with apitegromab-mstn exposures (AUC) lower than that in humans at the MRHD.

14 CLINICAL STUDIES

The efficacy of ISEMBYLD for the treatment of spinal muscular atrophy (SMA) in patients 2 years of age and older was demonstrated in a randomized, double-blind, placebo-controlled, multicenter clinical trial (Study 1; NCT05156320).

Study 1 enrolled a total of 188 patients with a diagnosis of 5q SMA who were 2 to 21 years of age. Patients were randomized in a 1:1:1 ratio to receive ISEMBYLD 20 mg/kg (twice the recommended dosage), ISEMBYLD 10 mg/kg (the recommended dosage), or placebo, respectively, via intravenous infusion once every 4 weeks for approximately 1 year. All patients enrolled in this trial were receiving an approved SMN2-targeted treatment (either nusinersen or risdiplam). All patients were nonambulatory at baseline.

In Study 1, the main efficacy population consisted of patients who were 2 to 12 years of age (n=156). Of the patients 2 to 12 years of age, 53 patients received at least one dose of ISEMBYLD 10 mg/kg (the recommended dosage) and 50 patients received placebo. Of these patients, the mean age was 8 years, 47% were female, 74% were White, 8% were of Hispanic or Latino ethnicity, 4% were Asian, and 2% were Black or African-American. Baseline disease characteristics including age of disease onset, disease duration, and Hammersmith Functional Motor Scale Expanded (HFMSE) scores were balanced between patients treated with ISEMBYLD and placebo. Ninety-nine percent of patients completed the study.

The primary efficacy endpoint was the mean change from baseline at 1 year in HFMSE, which evaluates motor function in patients with SMA. HFMSE is comprised of 33 scored activities that give objective information on motor ability and clinical progression, such as the ability to sit unassisted, stand, or walk. The item scores are summed for a total score, with a maximum of 66. A higher total score reflects better motor function.

ISEMBYLD at the recommended dosage of 10 mg/kg every 4 weeks demonstrated a nominally statistically significant treatment effect at 1 year on the HFMSE compared to placebo in patients with SMA 2 to 12 years of age (2.2 LS mean change versus placebo, p-value 0.01) (Table 2 and Figure 1). A greater proportion of patients treated with ISEMBYLD 10 mg/kg achieved 3 points or greater improvement on HFMSE at 1 year compared to placebo.

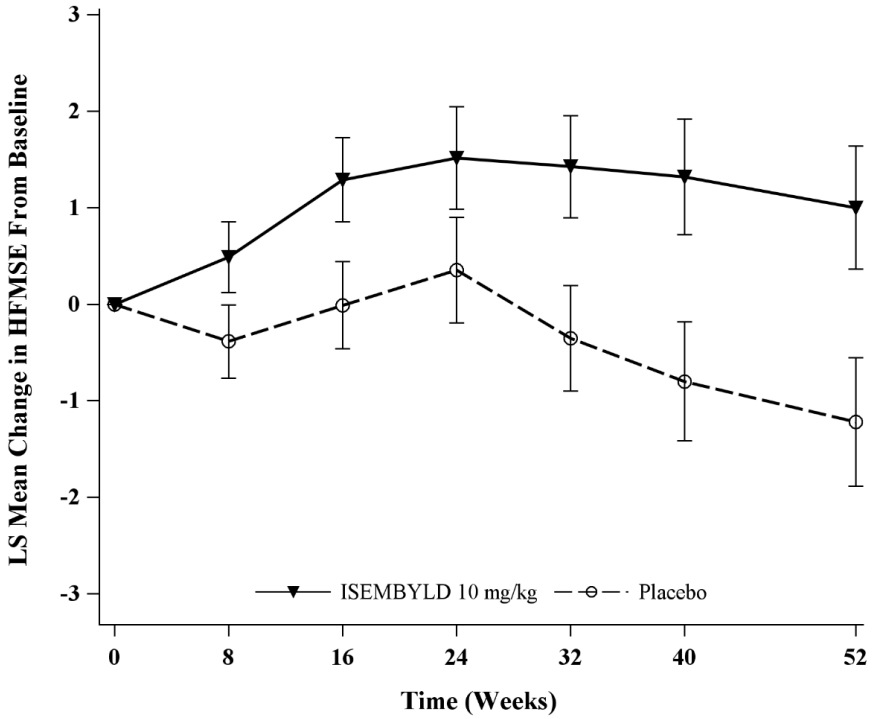
Efficacy assessments in patients with SMA 13 to 21 years of age receiving 20 mg/kg (twice the recommended dosage) of ISEMBYLD showed a trend consistent with the patients 2 to 12 years of age who received the 10 mg/kg dose. Further, the observed treatment effect of ISEMBYLD was similar across predefined subgroups.

Table 2: Summary of Efficacy in Patients with SMA at 1 Year of Treatment (Study 1)

Endpoint	**ISEMBYLD[1] 10 mg/kg (N = 53)**	**Placebo[1] (N = 50)**
Primary Endpoint:		
Change from baseline in HFMSE total score at 1 year	1.0	-1.2
Difference from placebo, LS mean difference (95% CI) p-value[2,3]	2.2 (0.49, 3.95) 0.0121	
Key Secondary Endpoints:		
Proportion of patients with a change from baseline in HFMSE total score of 3 or more at 1 year[4]	34.2%	13.5%
Odds ratio for overall response (95% CI) p-value[2,4]	3.8 (1.33, 10.90) 0.0125	

[1] All patients on SMN2-targeted treatment and 2 to 12 years of age.
[2] nominal p-value
[3] The MMRM analysis included the fixed effects of treatment group, visit, treatment group-by-visit interaction, baseline HFMSE total score, baseline HFMSE total score-by-visit interaction, and type of SMN Therapy (i.e., nusinersen or risdiplam).
[4] The Logistic regression model included covariates of Baseline HFMSE total score, and type of SMN Therapy (i.e., nusinersen or risdiplam). Analysis is based on imputed data when there are missing HFMSE total scores.
Abbreviations: CI, confidence interval; HFMSE, Hammersmith Functional Motor Scale Expanded; LS, least squares; MMRM, Mixed Model Repeated Measure; N, number of subjects; SMA, spinal muscular atrophy; SMN, survival motor neuron.

Figure 1: Mean Change from Baseline in HFMSE Total Score in Patients Aged 2 to 12 Years with SMA Through Year 1 (Study 1)



All patients on SMN2-targeted treatment.
Abbreviations: HFMSE, Hammersmith Functional Motor Scale Expanded; LS, Least Squares; SE, Standard Error; SMA, spinal muscular atrophy.
Note: Error bars represent +/- SE around the mean.

16 HOW SUPPLIED/STORAGE AND HANDLING

16.1 How Supplied

ISEMBYLD (apitegromab-mstn) injection is a clear to moderately opalescent, colorless to slightly yellow solution. It is supplied as one 150 mg/3 mL (50 mg/mL) single-dose glass vial per carton (NDC 84717-150-01).

16.2 Storage and Handling

Store ISEMBYLD vials in a refrigerator between 2°C to 8°C (36°F to 46°F) in the original carton to protect from light. Do not freeze. Do not shake. Discard unused portion.

For storage of the diluted infusion solution, see Dosage and Administration (2.3).

17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Patient Information).

Missed Dose Instructions

Inform patients that if a planned dose is missed, they should either:

- have ISEMBYLD administered as soon as possible and then maintain the regular dosing schedule 4 weeks after the missed dose is given, or
- the dose can be skipped and the next dose can be given as originally scheduled *[see Dosage and Administration (2.2)]*.

Fractures

Inform patients that ISEMBYLD may increase the risk of fractures, some of which can be serious *[see Warnings and Precautions (5.1)]*.

Manufactured by:
Scholar Rock, Inc.
301 Binney Street
Cambridge, MA 02142 USA
U.S. License No.: 2372

PATIENT INFORMATION
ISEMBYLD™ (*eye-SEM-bild*)
(apitegromab-mstn)
injection, for intravenous use

What is ISEMBYLD?
ISEMBYLD is a prescription medicine used to treat spinal muscular atrophy (SMA) in adults and children 2 years of age and older who are currently receiving a survival motor neuron 2 (SMN2) targeted treatment.
It is not known if ISEMBYLD is safe and effective in children under 2 years of age.

Before taking ISEMBYLD, tell your healthcare provider about all of your medical conditions, including if you:
- have a history of low bone density or bone fractures.
- are pregnant or plan to become pregnant. If you are pregnant or are planning to become pregnant, ask your healthcare provider for advice before taking this medicine. It is not known if ISEMBYLD will harm your unborn baby. Tell your healthcare provider right away if you become pregnant during treatment with ISEMBYLD.
- are breastfeeding or plan to breastfeed. It is not known if ISEMBYLD passes into breast milk. Talk to your healthcare provider about the best way to feed your baby while on treatment with ISEMBYLD.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. Keep a list of them to show your healthcare provider, including your pharmacist, when you get a new medicine.

How will I receive ISEMBYLD?
- You will receive ISEMBYLD from a healthcare provider through a needle placed in a vein (intravenous or IV infusion). The infusion will take about 1 to 2 hours to give you the full dose of medicine.
- You will receive ISEMBYLD every 4 weeks.
- Do not stop treatment with ISEMBYLD unless your healthcare provider tells you to.
- Your healthcare provider will determine the amount of ISEMBYLD needed based on your current weight.
- If you miss a dose of ISEMBYLD, either:
    - ISEMBYLD should be given (administered) as soon as possible and then restart the dosing schedule 4 weeks after the missed dose is given, or
    - the dose can be skipped and the next dose can be given as originally scheduled.

What are the possible side effects of ISEMBYLD?
- **Fractures.** Treatment with ISEMBYLD may increase the risk of bone fractures, including serious fractures. Bone fractures may happen with or without a fall or other injury. Your healthcare provider may consider stopping treatment with ISEMBYLD if you experience a bone fracture during treatment.

The most common side effects of ISEMBYLD include:
- upper respiratory tract infections
- vomiting
- cough
- viral infections
- headache
- stomach flu (gastroenteritis)
- sore throat (pharyngitis)
- hypersensitivity

These are not all of the possible side effects of ISEMBYLD. Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

General information about the safe and effective use of ISEMBYLD.
Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet.
You can ask your pharmacist or healthcare provider for information about ISEMBYLD that is written for health professionals.

What are the ingredients in ISEMBYLD?
Active ingredients: apitegromab-mstn
Inactive ingredients: histidine, L-histidine hydrochloride monohydrate, sodium chloride, polysorbate 80, and Water for Injection. Hydrochloric acid was added to adjust the pH.

Manufactured by: Scholar Rock, Inc., 301 Binney St, Cambridge, MA 02142 USA. U.S. License No. 2372

For more information, go to www.ISEMBYLD.com or call 1-877-ISEMBYLD (1-877-473-6295).

This Patient Information has been approved by the U.S. Food and Drug Administration Issued: 9/2026