

# **ABRYSVO Powder and Solvent for Solution for Injection**

## **1 DESCRIPTION**

ABRYSVO (Respiratory Syncytial Virus Vaccine) is a sterile solution for intramuscular injection. The vaccine is supplied as a vial of Lyophilized Antigen Component that is reconstituted at the time of use with a Sterile Water Diluent Component. The antigen component contains recombinant RSV preF A and RSV preF B.

The RSV preF A and RSV preF B recombinant proteins are expressed in genetically engineered Chinese Hamster Ovary cell lines grown in suspension culture using chemically-defined media, without antibiotics or animal-derived components. The recombinant proteins are purified through a series of column chromatography and filtration steps followed by formulation, filling into vials, and lyophilization.

After reconstitution, each dose of ABRYSVO is approximately 0.5 mL. The vaccine is formulated to contain 120 mcg of RSV stabilized prefusion F proteins (60 mcg RSV preF A and 60 mcg RSV preF B) per 0.5 mL. ABRYSVO also contains the following buffer ingredients: 0.11 mg tromethamine, 1.04 mg tromethamine hydrochloride, 11.3 mg sucrose, 22.5 mg mannitol, 0.08 mg polysorbate 80, and 1.1 mg sodium chloride per 0.5 mL. ABRYSVO is a sterile, clear, and colorless solution.

ABRYSVO contains no preservatives. Each dose may also contain residual amounts of host cell proteins ( $\leq 0.1\%$  w/w) and DNA ( $< 0.4$  ng/mg of total protein) from the manufacturing process.

The vial stopper and tip cap and rubber plunger of the prefilled syringe are not made with natural rubber latex.

## **2 INDICATIONS AND USAGE**

### **2.1 Immunization of Pregnant Individuals**

ABRYSVO is a vaccine indicated for active immunization of pregnant individuals at 32 through 36 weeks gestational age for the prevention of lower respiratory tract disease (LRTD) and severe LRTD caused by respiratory syncytial virus (RSV) in infants from birth through 6 months of age.

### **2.2 Immunization of Individuals 60 Years of Age and Older**

ABRYSVO is a vaccine indicated for active immunization for the prevention of LRTD caused by RSV in individuals 60 years of age and older.

## **3 DOSAGE AND ADMINISTRATION**

### **3.1 Dose and Schedule**

Administer a single dose (approximately 0.5 mL) of ABRYSVO intramuscularly.

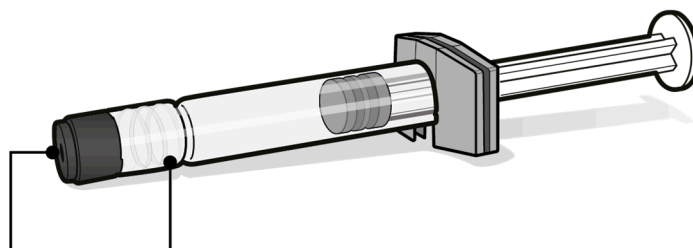
### 3.2 Preparation for Administration

The lyophilized vaccine (powder) must be reconstituted only with the diluent provided to form ABRYSVO.

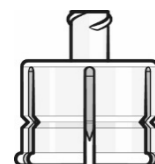
**Vial containing lyophilized RSV preF vaccine**



**Syringe containing diluent**



**Vial adapter**



**Syringe cap**

**Luer lock adapter**



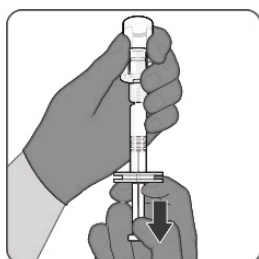
#### **Step 1. Attach vial adapter**

- Peel off the top cover from the vial adapter packaging and remove the flip off cap from the vial.
- While keeping the vial adapter in its packaging, center over the vial's stopper and connect with a straight downward push. Do not push the vial adapter in at an angle as it may result in leaking. Remove the packaging.



#### **Step 2. Reconstitute lyophilized vaccine component to form ABRYSVO**

- For all syringe assembly steps, hold the syringe only by the Luer lock adapter. This will prevent the Luer lock adapter from detaching during use.
- Twist to remove the syringe cap, then twist to connect the syringe to the vial adapter. Stop turning when you feel resistance.
- Inject the entire contents of the syringe into the vial. Hold the plunger rod down and gently swirl the vial until the powder is completely dissolved. Do not shake.



#### **Step 3. Withdraw reconstituted vaccine**

- Invert the vial completely and slowly withdraw the entire contents into the syringe to ensure a 0.5 mL dose of ABRYSVO.
- Twist to disconnect the syringe from the vial adapter.
- Attach a sterile needle suitable for intramuscular injection.

Reconstituted vaccine for administration

The prepared vaccine is a clear and colorless solution. Visually inspect the vaccine for large particulate matter and discoloration prior to administration. Do not use if large particulate matter or discoloration is found.

### Disposal

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

## **3.3 Administration**

### **For intramuscular injection only.**

After reconstitution, administer ABRYSV0 immediately or store at room temperature (15°C to 30°C) and use within 4 hours. Discard reconstituted vaccine if not used within 4 hours.

## **4 DOSAGE FORMS AND STRENGTHS**

ABRYSV0 is a solution for injection. A single dose after reconstitution is approximately 0.5 mL.

## **5 CONTRAINDICATIONS**

Do not administer ABRYSV0 to individuals with a history of a severe allergic reaction (e.g., anaphylaxis) to any component of ABRYSV0 [see *Description (1)*].

## **6 WARNINGS AND PRECAUTIONS**

### **6.1 Potential Risk of Preterm Birth**

A numerical imbalance in preterm births in ABRYSV0 recipients was observed compared to placebo recipients in two clinical studies [see *Adverse Reactions (7.1)*]. Available data are insufficient to establish or exclude a causal relationship between preterm birth and ABRYSV0. To avoid the potential risk of preterm birth with use of ABRYSV0 before 32 weeks of gestation, administer ABRYSV0 as indicated in pregnant individuals at 32 through 36 weeks gestational age. Pregnant individuals who were at increased risk of preterm birth were generally excluded from clinical studies of ABRYSV0.

### **6.2 Management of Acute Allergic Reactions**

Appropriate medical treatment used to manage immediate allergic reactions must be immediately available in the event an anaphylactic reaction occurs following administration of ABRYSV0.

### **6.3 Syncope**

Syncope (fainting) may occur in association with administration of injectable vaccines, including ABRYSV0. Procedures should be in place to avoid injury from fainting.

## 6.4 Altered Immunocompetence

Immunocompromised individuals, including those receiving immunosuppressive therapy, may have a diminished immune response to ABRYSV0.

## 6.5 Limitations of Vaccine Effectiveness

Vaccination with ABRYSV0 may not protect all vaccine recipients.

## 7 ADVERSE REACTIONS

In pregnant individuals, the most commonly reported ( $\geq 10\%$ ) adverse reactions were pain at the injection site (40.6%), headache (31.0%), muscle pain (26.5%), and nausea (20.0%).

In individuals 60 years of age and older, the most commonly reported ( $\geq 10\%$ ) adverse reactions were fatigue (15.5%), headache (12.8%), pain at the injection site (10.5%), and muscle pain (10.1%).

### 7.1 Clinical Trials Experience

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

#### Pregnant Individuals and Infants from Birth Through 6 Months of Age

The safety of ABRYSV0 in maternal and infant participants was evaluated in two clinical studies in which approximately 4,000 maternal participants received a single dose of ABRYSV0.

Study 1 (NCT04424316) is an ongoing, Phase 3, randomized, double-blind, multicenter, placebo-controlled study to investigate the efficacy and safety of ABRYSV0 administered to pregnant individuals  $\leq 49$  years of age with uncomplicated, singleton pregnancies, to protect their infants against RSV disease. Pregnant individuals with high-risk pregnancies were excluded from the study (BMI  $> 40$  kg/m<sup>2</sup> prior to pregnancy, pregnancies resulting after in vitro fertilization, pre-eclampsia, eclampsia, uncontrolled gestational hypertension, placental abnormalities, polyhydramnios or oligohydramnios, significant bleeding or blood clotting disorder, unstable endocrine disorders including untreated disorders of glucose intolerance or thyroid disorders). Pregnant individuals with prior pregnancy complications (e.g., history of preterm birth  $\leq 34$  weeks gestation, prior stillbirth, neonatal death, previous infant with a known genetic disorder or significant congenital anomaly) could be included, based on the investigators' judgment, but were generally not enrolled in the study. In this study with 1:1 randomization 3,682 participants received ABRYSV0 and 3,675 received placebo (0.5 mL dose, containing the same buffer ingredients in the same quantities as in a single dose of ABRYSV0 [see Description (1)]). Infants born in year 1 are to be followed for up to 24 months, and infants born in year 2 will be followed for up to 12 months to assess safety. At the time of data evaluation following a median of 8.9 months (range Day 1-23.8 months), 3,568 infants were born to the maternal participants in the ABRYSV0 group and 3,558 in the placebo group, and of these, approximately 45.6% have been followed for 12 months. This multicenter study is being conducted in Argentina, Australia, Brazil, Canada, Chile,

Denmark, Finland, Gambia, Japan, Republic of Korea, Mexico, Netherlands, New Zealand, Philippines, South Africa, Spain, Taiwan, and the US.

Demographic characteristics in Study 1 among participants who received ABRYSV0 and those who received placebo were generally similar with regard to age, race, and ethnicity. Of the participants in the study, 65% were White, 20% were Black or African American, 13% were Asian, and 29% were Hispanic/Latino. The median maternal age at the time of study vaccination was 29 years (range 16 to 45 years in the ABRYSV0 group, 14 to 47 years in the placebo group). The median gestational age at vaccination was 31 weeks and 2 days (range 24-36.9 weeks). ABRYSV0 is approved for use for pregnant individuals at 32 through 36 weeks gestational age [see *Indications and Usage (2.1)*]. The median infant gestational age at birth was 39 weeks and 1 day (range 27 weeks and 3 days to 44 weeks and 2 days). Among the infants born to maternal participants 51% were male and 49% were female.

Study 2 (NCT04032093) was a Phase 2, randomized, placebo-controlled, observer-blinded study that investigated the safety of two dose levels (120 mcg and a higher dose) of ABRYSV0 administered to pregnant individuals. ABRYSV0 (120 mcg) was administered to 115 maternal participants, and 114 infants were born to these maternal participants. This study was conducted in the US, South Africa, Argentina, and Chile. Demographic characteristics among participants who received ABRYSV0 and those who received placebo were generally similar with regard to age, race, and ethnicity. Of the participants in the study, 76% were White, 21% were Black or African American, and 28% were Hispanic/Latino. The median age of participants was 27 years (range 18-42 years). The median gestational age at vaccination was 30 weeks (range 24-36 weeks). ABRYSV0 is approved for use for pregnant individuals at 32 through 36 weeks gestational age [see *Indications and Usage (2.1)*].

For all maternal participants in Study 1, solicited local reactions and systemic events were collected using electronic diaries for 7 days after study vaccination, adverse events for 1 month and obstetric complications, serious adverse events, and adverse events of special interest for the duration of the study. For infant participants, the collection period for nonserious adverse events was from birth to 1 month. Serious adverse events were monitored for at least 1 year for all infant participants and for up to 2 years for half of the infants in Study 1.

#### *Solicited Local and Systemic Reactions in Study 1*

The majority of solicited local and systemic reactions in maternal participants resolved within 2-3 days of onset. Severe local reactions were reported for 0.3% of maternal participants in the ABRYSV0 group and none in the placebo group, and severe systemic reactions within 7 days after vaccination were reported by 2.3% of maternal participants in both groups.

Solicited local and systemic reactions reported within 7 days after vaccination in Study 1 are presented in Tables 1 and 2.

**Table 1 Percentage of Maternal Participants with Local Reactions Reported, by Maximum Severity, within 7 Days after Vaccination – Study 1<sup>a</sup>**

Local Reactions	ABRYSVO N=3,663 <sup>b</sup> %	PLACEBO N=3,639 <sup>b</sup> %
Injection site pain <sup>c</sup>		
Any <sup>d</sup>	40.6	10.1
Mild	36.1	9.3
Moderate	4.4	0.9
Severe	0.1	0
Redness <sup>c</sup>		
Any <sup>d</sup>	7.2	0.2
Mild	5.0	0.1
Moderate	2.1	0.1
Severe	0.1	0
Swelling <sup>c</sup>		
Any <sup>d</sup>	6.2	0.2
Mild	4.1	0.1
Moderate	2.0	<0.1
Severe	<0.1	0

<sup>a</sup> NCT04424316.

<sup>b</sup> N = number of participants who provided e-diary data for a specific reaction after vaccination.

<sup>c</sup> Mild: does not interfere with activity; moderate: interferes with activity; severe: prevents daily activity.

<sup>d</sup> Any includes all participants who reported a reaction as mild, moderate, or severe during Day 1 to Day 7 after vaccination.

<sup>e</sup> Mild: >2 cm to 5 cm; moderate: >5 cm to 10 cm; severe: >10 cm.

**Table 2 Percentage of Maternal Participants with Systemic Reactions Reported, by Maximum Severity, within 7 Days after Vaccination – Study 1<sup>a</sup>**

Systemic Reactions	ABRYSVO N=3,663 <sup>b</sup> %	PLACEBO N=3,638-3,639 <sup>b</sup> %
Fever (≥38.0°C)		
≥38.0°C	2.6	2.9
≥38.0°C to 38.4°C	1.7	1.5
>38.5°C to 38.9°C	0.8	1.2
>39.0°C to 40.0°C	<0.1	0.1
>40.0°C	<0.1	0.1
Fatigue <sup>c</sup>		
Any <sup>d</sup>	46.1	43.8
Mild	23.4	22.8
Moderate	21.4	19.6
Severe	1.3	1.4
Headache <sup>c</sup>		
Any <sup>d</sup>	31.0	27.6
Mild	20.2	17.9
Moderate	10.4	9.3
Severe	0.4	0.4

<b>Systemic Reactions</b>	<b>ABRYSVO N=3,663<sup>b</sup> %</b>	<b>PLACEBO N=3,638-3,639<sup>b</sup> %</b>
<b>Muscle pain<sup>c</sup></b>		
Any <sup>d</sup>	26.5	17.1
Mild	17.6	10.0
Moderate	8.6	6.8
Severe	0.4	0.3
<b>Nausea<sup>c</sup></b>		
Any <sup>d</sup>	20.0	19.2
Mild	14.4	13.8
Moderate	5.4	5.2
Severe	0.2	0.2
<b>Joint pain<sup>c</sup></b>		
Any <sup>d</sup>	11.6	10.5
Mild	6.5	6.0
Moderate	4.9	4.4
Severe	0.2	<0.1
<b>Diarrhea<sup>c</sup></b>		
Any	11.2	11.5
Mild	9.1	9.4
Moderate	2.0	1.9
Severe	0.1	0.2
<b>Vomiting<sup>f</sup></b>		
Any	7.8	7.0
Mild	6.4	5.4
Moderate	1.3	1.5
Severe	0.2	<0.1

<sup>a</sup> NCT04424316.

<sup>b</sup> N = number of participants who provided e-diary data for a specific reaction after vaccination.

<sup>c</sup> Mild: does not interfere with activity; moderate: some interference with activity; severe: prevents daily routine activity.

<sup>d</sup> Any includes all participants who reported a reaction as mild, moderate, or severe during Day 1 to Day 7 after vaccination.

<sup>e</sup> Mild: 2 to 3 loose stools in 24 hours; moderate: 4 to 5 loose stools in 24 hours; severe: 6 or more loose stools in 24 hours.

<sup>f</sup> Mild: 1 to 2 times in 24 hours; moderate: >2 times in 24 hours; severe: requires intravenous hydration.

### Unsolicited Adverse Events in Study 1

Unsolicited adverse events reported within 1 month after vaccination by maternal participants were 13.7% in the ABRYSVO group and 13.1% in the placebo group.

The most frequently reported unsolicited adverse events in maternal participants from vaccination through the 1-month follow-up visit were disorders of pregnancy, puerperium and perinatal conditions (7.0% for the ABRYSVO group versus 6.2% for the placebo group).

### Serious Adverse Events in Study 1

In Study 1, serious adverse events in maternal participants were reported by 16.2% in the ABRYSVO group and 15.2% in the placebo group occurring any time during the study (see Table 3) with 4.2% serious adverse events in the ABRYSVO group and 3.7% in the placebo group occurring within 1 month after vaccination. Most of the serious adverse events in maternal participants were related to pregnancy complications and occurred after the 1-month period following vaccination.

**Table 3 Select Pregnancy-related Serious Adverse Events in Study 1 in Pregnant Individuals Occurring at any Time Following Vaccination<sup>a</sup>**

Serious Adverse Reaction	ABRYSVO N=3,682 n (%)	95% CI	Placebo N=3,675 n (%)	95% CI
All Maternal SAEs	598 (16.2)	(15.1, 17.5)	558 (15.2)	(14.0, 16.4)
Pre-eclampsia	68 (1.8)	(1.4, 2.3)	53 (1.4)	(1.1, 1.9)
Gestational hypertension	41 (1.1)	(0.8, 1.5)	38 (1.0)	(0.7, 1.4)
Premature rupture of membranes	15 (0.4)	(0.2, 0.7)	16 (0.4)	(0.2, 0.7)
Preterm premature rupture of membranes	15 (0.4)	(0.2, 0.7)	10 (0.3)	(0.1, 0.5)
Hypertension	13 (0.4)	(0.2, 0.6)	6 (0.2)	(0.1, 0.4)
Maternal death <sup>b</sup>	1 (<0.1)	(0.0, 0.2)	0	(0.0, 0.1)
Fetal Death <sup>c</sup>	10 (0.3)	(0.1, 0.5)	8 (0.2)	(0.1, 0.4)

<sup>a</sup> Includes all SAEs from vaccination to 6 months post-delivery (up to approximately 10 months, depending on the gestational age at the time of vaccination). In Study 1, eclampsia occurred in 5 participants (3 in the ABRYSVO group and 2 in the placebo group) and HELLP syndrome occurred in 5 participants (2 in the ABRYSVO group and 3 in the placebo group).

<sup>b</sup> There was one maternal death in the ABRYSVO group due to postpartum hemorrhage that was not likely to be associated with vaccination.

<sup>c</sup> A total of 18 intrauterine deaths were reported for the index pregnancy: 10 intrauterine deaths in the ABRYSVO group (0.3%) and 8 intrauterine deaths in the placebo group (0.2%). The intrauterine deaths represented various clinical conditions and presentations resulting in fetal demise without clear evidence of a common pathophysiology.

### Preterm Births in Study 1 and Study 2

A numerical imbalance in preterm births in ABRYSVO recipients compared to placebo recipients was observed in both Studies 1 and 2. In Study 2, preterm births occurred in 5.3% (6 out of 114) in the ABRYSVO group and 2.6% (3 out of 116) in the placebo group. In the subsequent Study 1, preterm birth events occurred in 5.7% [95% CI: 4.9, 6.5] (202 out of 3,568) in the ABRYSVO group and 4.7% [95% CI: 4.1, 5.5] (169 out of 3,558) in the placebo group. In infants born preterm, 83 infants in the ABRYSVO group and 80 infants in the placebo group remained hospitalized or were readmitted to the hospital in the neonatal period (up to 30 days after birth). Available data are insufficient to establish or exclude a causal relationship between preterm birth and ABRYSVO.

A numerical imbalance in preterm births was also observed in Study 1 among the subgroup of infants born to participants who were vaccinated at 32 through 36 weeks gestation, with 4.2% (68/1,631) in the ABRYSVO group and 3.7% (59/1,610) in the placebo group.



### Adverse Reactions in Infants

In Study 1, adverse events in infants from birth to 1 month of age were observed in 37.1% in the ABRYSVO group compared to 34.5% in the placebo group. Low birth weight was observed in 5.1% of participants in the ABRYSVO group versus 4.4% in the placebo group, and neonatal jaundice was observed in 7.2% in the ABRYSVO group versus 6.7% in the placebo group.

### Individuals 60 Years of Age and Older

The safety of ABRYSVO was evaluated in Study 3 (NCT05035212) in which 17,215 participants received ABRYSVO and 17,069 received placebo (0.5 mL dose, containing the same buffer ingredients in the same quantities as in a single dose of ABRYSVO [see *Description (1)*]). Study 3 is an ongoing, multicenter, randomized, double-blind, placebo-controlled study to assess the efficacy and safety of ABRYSVO in individuals 60 years of age and older. This study is being conducted in the US, Argentina, Japan, the Netherlands, Canada, South Africa, and Finland. Demographic characteristics among participants who received ABRYSVO and those who received placebo were generally similar with regard to age, sex, race, and ethnicity. Of the participants in the study, 51% were male and 78% were White, 13% were Black or African American, and 37% were Hispanic/Latino. The median age of participants was 67 years (range 59-97 years).

Solicited local and systemic reactions were collected using electronic diaries for 7 days after study vaccination in 7,169 participants (3,630 ABRYSVO participants and 3,539 placebo recipients) from a subset of sites. For all participants, unsolicited adverse events were collected for one month after study vaccination; serious adverse events (SAEs) are collected throughout study participation.

### Solicited Local and Systemic Reactions in Study 3

Solicited local and systemic reactions reported within 7 days after vaccination in Study 3 are presented in Tables 4 and 5.

**Table 4 Percentage of Participants 60 Years of Age and Older with Local Reactions Reported, by Maximum Severity, within 7 Days after Vaccination – Study 3<sup>a</sup>**

Local Reactions	ABRYSVO N=3,619-3,621 <sup>b</sup> %	PLACEBO N=3,532-3,539 <sup>b</sup> %
Injection site pain <sup>c</sup>		
Any <sup>d</sup>	10.5	6.0
Mild	9.4	5.3
Moderate	1.1	0.7
Severe	<0.1	0
Redness <sup>d,e</sup>		
Any <sup>d</sup>	2.7	0.7
Mild	1.5	0.5
Moderate	1.1	0.2
Severe	0.1	0

Swelling <sup>d,e</sup>		
Any <sup>d</sup>	2.4	0.5
Mild	1.5	0.2
Moderate	0.9	0.2
Severe	0.1	<0.1

<sup>a</sup> NCT05035212.

<sup>b</sup> N = number of participants who provided e-diary data for a specific reaction after vaccination.

<sup>c</sup> Mild: does not interfere with activity; moderate: some interference with activity; severe: prevents daily activity.

<sup>d</sup> Any includes all participants who reported a reaction as mild, moderate, or severe during Day 1 to Day 7 after vaccination.

<sup>e</sup> Mild: 2.5 cm to 5 cm; moderate: >5 cm to 10 cm; severe: >10 cm (for data reported from e-diaries).

**Table 5 Percentage of Participants 60 Years of Age and Older with Systemic Reactions Reported, by Maximum Severity, within 7 Days after Vaccination – Study 3<sup>a</sup>**

Systemic Reactions	ABRYSVO N=3,619-3,621 <sup>b</sup> %	PLACEBO N=3,532-3,539 <sup>b</sup> %
Fever (≥38.0°C)		
≥38.0°C	1.4	1.4
≥38.0°C to 38.4°C	0.6	0.8
>38.4°C to 38.9°C	0.8	0.6
>38.9°C to 40.0°C	<0.1	<0.1
>40.0°C	0	<0.1
Fatigue <sup>c</sup>		
Any <sup>d</sup>	15.5	14.4
Mild	9.3	8.4
Moderate	5.9	5.8
Severe	0.3	0.1
Headache <sup>c</sup>		
Any <sup>d</sup>	12.8	11.7
Mild	9.0	8.4
Moderate	3.7	3.2
Severe	0.1	<0.1
Muscle pain <sup>c</sup>		
Any <sup>d</sup>	10.1	8.4
Mild	6.5	5.5
Moderate	3.5	2.8
Severe	0.2	<0.1
Joint pain <sup>c</sup>		
Any <sup>d</sup>	7.5	6.9
Mild	4.5	3.9
Moderate	2.9	2.9
Severe	<0.1	<0.1
Nausea <sup>c</sup>		
Any <sup>d</sup>	3.4	3.7
Mild	2.5	3.1

<b>Systemic Reactions</b>	<b>ABRYSVO N=3,619-3,621<sup>b</sup> %</b>	<b>PLACEBO N=3,532-3,539<sup>b</sup> %</b>
Moderate	0.9	0.6
Severe	0	<0.1
<b>Vomiting<sup>e</sup></b>		
Any <sup>d</sup>	0.9	0.8
Mild	0.7	0.7
Moderate	0.2	0.1
Severe	0	<0.1
<b>Diarrhea<sup>f</sup></b>		
Any <sup>d</sup>	5.9	5.2
Mild	4.4	4.2
Moderate	1.3	0.9
Severe	0.1	0.1

<sup>a</sup> NCT05035212.

<sup>b</sup> N = number of participants who provided e-diary data for a specific reaction after vaccination.

<sup>c</sup> Mild: does not interfere with activity; moderate: some interference with activity; severe: prevents daily routine activity.

<sup>d</sup> Any includes all participants who reported a reaction as mild, moderate, or severe during Day 1 to Day 7 after vaccination.

<sup>e</sup> Mild: 1 to 2 times in 24 hours; moderate: >2 times in 24 hours; severe: requires intravenous hydration.

<sup>f</sup> Mild: 2 to 3 loose stools in 24 hours; moderate: 4 to 5 loose stools in 24 hours; severe: 6 or more loose stools in 24 hours.

Solicited local and systemic reactions had a median duration of 1-2 days.

### Unsolicited Adverse Events in Study 3

Unsolicited adverse events occurring within 1 month after vaccination were similar between groups, reported in 8.9% and 8.5% of participants who received ABRYSVO and placebo, respectively.

Within 30 days after vaccination, atrial fibrillation was reported in 10 vaccine recipients and 4 placebo recipients (of which 4 in the ABRYSVO group and 3 in the placebo group were serious adverse events); the onset of symptoms was 18 to 30 days post vaccination. The currently available information on atrial fibrillation is insufficient to determine a causal relationship to the vaccine. There were no other notable patterns or numerical imbalances between groups for specific categories of unsolicited adverse events.

### Serious Adverse Events in Study 3

In Study 3, SAEs were reported by 2.3% of participants in both the ABRYSVO and placebo groups. Three participants in the ABRYSVO group had SAEs which were assessed as possibly related to study vaccination: Guillain-Barre Syndrome reported 7 days after vaccination, Miller Fisher Syndrome reported 8 days after vaccination, and hypersensitivity reported 8 hours after vaccination.

## 8 DRUG INTERACTIONS

In Study 4 in a concomitant administration study of ABRYSSVO and a Tetanus Toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis Vaccine, Adsorbed (Tdap) in non-pregnant women, no safety concerns were identified. Immune responses to RSV A, RSV B, diphtheria, and tetanus were non-inferior to those after separate administration. Lower geometric mean antibody concentrations (GMCs) to the acellular pertussis antigens (pertussis toxin [PT], filamentous hemagglutinin [FHA], and pertactin [PRN]) were measured when ABRYSSVO was administered concomitantly with Tdap compared to pertussis GMCs when Tdap was administered alone [see *Clinical Studies (12.3)*].

Concomitant administration of Tdap with ABRYSSVO in pregnant individuals has not been studied.

## 9 USE IN SPECIFIC POPULATIONS

### 9.1 Pregnancy

#### Risk Summary

All pregnancies have a risk of birth defect, loss, or other adverse outcomes. In the US general population, the estimated background risk of major birth defects and miscarriages in clinically recognized pregnancies is 2% to 4%, and 15% to 20%, respectively, and the estimated background risk of fetal deaths after 20 weeks is 0.6%.

Study 1 enrolled 7,358 pregnant individuals who were randomized 1:1 and received ABRYSSVO or placebo (0.5 mL dose, containing the same buffer ingredients in the same quantities as in a single dose of ABRYSSVO [see *Description (1)*]) revealed no evidence for vaccine-associated increase in the risk of congenital anomalies or fetal deaths. Study 2 evaluated 115 pregnant individuals who received ABRYSSVO and 117 who received placebo. A numerical imbalance in preterm births in ABRYSSVO recipients was observed compared to placebo recipients in these two clinical studies. Available data are insufficient to establish or exclude a causal relationship between preterm birth and ABRYSSVO [see *Warnings and Precautions (6.1)*, *Adverse Reactions (7.1)*, *Clinical Considerations (9.1)*, *Data (9.1)* and *Clinical Studies (12.1)*].

A developmental toxicity study was performed in female rabbits administered a vaccine formulation containing two times the antigen content of a single human dose of ABRYSSVO prior to and during gestation. The study showed no evidence of harm to the fetus or to postnatal survival, growth, or development (see *Animal Data*).

#### Clinical Considerations

##### Maternal Adverse Reactions

In Study 1, 3,682 pregnant individuals received ABRYSSVO and 3,676 received placebo. Local and systemic adverse reactions occurred with greater frequency in the ABRYSSVO group. Serious adverse reactions observed in pregnant individuals at a higher rate in the ABRYSSVO group compared to the placebo group included pre-eclampsia (1.8% versus 1.4%) and gestational hypertension (1.1% versus 1.0%) [see *Adverse Reactions (7.1)*].

ABRYSVO has not been studied in pregnant individuals less than 24 weeks gestational age, and those at increased risk for preterm birth.

### Fetal/Neonatal Adverse Reactions

The infant safety population included 3,568 and 3,558 infants born to individuals in the ABRYSVO or placebo group, respectively. There were 10 (0.3%) fetal deaths in the ABRYSVO group and 8 (0.2%) in the placebo group. Among the infants born to individuals in the ABRYSVO group and in the placebo group, 202 (5.7%) and 169 (4.7%), respectively, were born preterm [see *Warnings and Precautions (6.1)*, *Adverse Reactions (7.1)* and *Clinical Studies (12.1)*]. Low birth weight was observed in 5.1% of participants in the ABRYSVO group versus 4.4% in the placebo group, and neonatal jaundice was observed in 7.2% in the ABRYSVO group versus 6.7% in the placebo group [see *Adverse Reactions (7.1)*]. For mortality in the neonatal period among infants born to pregnant individuals in Study 1, there were 2 deaths in the ABRYSVO group and 5 in the placebo group, and for overall mortality including after the neonatal period there were 5 deaths in the ABRYSVO group and 12 in the placebo group. Congenital abnormalities were reported in 5.0% in the ABRYSVO group and 6.2% in the placebo group.

Available data are insufficient to establish or exclude a causal relationship between preterm birth and ABRYSVO. To avoid the potential risk of preterm birth with use of ABRYSVO before 32 weeks of gestation, administer ABRYSVO as indicated in pregnant individuals at 32 through 36 weeks gestational age.

### Data

#### Human Data

In Study 1, 3,682 pregnant individuals received ABRYSVO and 3,676 received placebo at 24 through 36 weeks' gestation. The infant safety population included 3,568 and 3,558 infants born to individuals in the ABRYSVO or placebo group, respectively. Among the infants born to individuals in the ABRYSVO group and in the placebo group, 202 (5.7%) and 169 (4.7%), respectively, had adverse events of preterm birth and 180 (5.0%) and 220 (6.2%), respectively, had reported congenital malformations or anomalies. There were 10 (0.3%) fetal deaths in the ABRYSVO group and 8 (0.2%) in the placebo group.

#### Animal Data

A pre- and post-natal developmental toxicity study with an embryo-fetal developmental toxicity phase was performed in female New Zealand White rabbits. Rabbits were administered 4 doses by intramuscular injection: at 3 weeks and at 1 week prior to mating, and on gestation days 10 and 24. On each occasion, rabbits received 0.5 mL of a vaccine formulation containing twice the antigen content of F glycoproteins of RSV A and RSV B (120 mcg RSV preF A and 120 mcg RSV preF B), stabilized in prefusion conformation as contained in a single human dose of ABRYSVO [see *Description (1)*]. No adverse effects on mating, female fertility, or on embryo/fetal or post-natal survival, growth, or development were observed. There were no vaccine-related fetal malformations or variations.

## 9.2 Lactation

### Risk Summary

It is not known whether ABRYSV0 is excreted in human milk. Data are not available to assess the effects of ABRYSV0 on the breastfed infant or on milk production/excretion. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for ABRYSV0 and any potential adverse effects on the breastfed child from ABRYSV0 or from the underlying maternal condition. For preventative vaccines, the underlying maternal condition is susceptibility to disease prevented by the vaccine.

## 9.3 Pediatric Use

The safety and effectiveness of ABRYSV0 to prevent RSV-associated lower respiratory tract disease (RSV-LRTD) and severe RSV-LRTD in infants born to individuals vaccinated at younger than 10 years of age have not been established.

The safety and effectiveness of ABRYSV0 to prevent RSV-LRTD in non-pregnant individuals younger than 18 years of age via active immunization have not been established.

## 9.4 Geriatric Use

ABRYSV0 is approved for use in individuals 60 years of age and older. In Study 3, of the 17,215 recipients who received ABRYSV0 62% (n=10,756) were aged 60-69 years of age, 32% (n=5,488) were 70-79 years of age and 6% (n=970) were ≥80 years of age [*see Adverse Reactions (7.1) and Clinical Studies (12.1)*].

# 10 CLINICAL PHARMACOLOGY

## 10.1 Mechanism of Action

### Active Immunization

ABRYSV0 induces an immune response against RSV preF that protects against lower respiratory tract disease caused by RSV.

### Passive Immunization

Antibodies to RSV antigens from individuals vaccinated in pregnancy are transferred transplacentally to protect infants younger than 6 months of age against LRTD and severe LRTD caused by RSV.

# 11 NONCLINICAL TOXICOLOGY

## 11.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

ABRYSV0 has not been evaluated for the potential to cause carcinogenicity, genotoxicity, or impairment of male fertility. A developmental toxicity study in female rabbits revealed no evidence of impaired female fertility after administration of a vaccine formulation containing

two times the antigen content of a single human dose of ABRYSSVO [see *Use in Specific Populations* (9.1)].

## 12 CLINICAL STUDIES

### 12.1 Study in Pregnant Individuals For Efficacy in Their Infants from Birth Through 6 Months of Age

Study 1 (NCT04424316) is a Phase 3 study that assessed the efficacy of ABRYSSVO in the prevention of RSV-associated lower respiratory tract disease (LRTD) in infants born to individuals vaccinated during pregnancy. The study evaluated the efficacy of ABRYSSVO to prevent RSV-associated LRTD and severe RSV-LRTD in infants within 90, 120, 150, and 180 days after birth. Participants were randomized (1:1) to receive ABRYSSVO (0.5 mL dose) or placebo (0.5 mL dose containing the same buffer ingredients in the same quantities as in a single dose of ABRYSSVO [see *Description* (1)]). This study includes sites in both the northern and southern hemispheres. Vaccine efficacy (VE) was defined as the relative risk reduction of the endpoints of severe LRTD caused by RSV and LRTD caused by RSV in infants born to individuals who received ABRYSSVO compared to infants born to individuals who received placebo. The demographic characteristics of Study 1 are described in Clinical Trials Experience Section 6.1.

Maternal participants were randomized (1:1) to receive ABRYSSVO (3,695) or placebo (3,697). RSV-associated LRTD in infants was defined as a medically attended visit with a reverse transcription-polymerase chain reaction (RT-PCR) confirmed RSV illness with one or more of the following respiratory symptoms: tachypnea (respiratory rate  $\geq 60$  breaths/minute [ $< 2$  months of age],  $\geq 50$  breaths/minute [ $\geq 2$  to 12 months of age], or  $\geq 40$  breaths/minute [ $\geq 12$ -24 months of age]); SpO<sub>2</sub> measured in room air  $< 95\%$ ; chest wall indrawing. RSV-associated severe LRTD was a subset defined as meeting the LRTD RSV criteria plus at least one of the following: tachypnea (respiratory rate  $\geq 70$  breaths per minute [ $< 2$  months of age],  $\geq 60$  breaths per minute [ $\geq 2$  to 12 months of age], or  $\geq 50$  bpm [ $\geq 12$  to 24 months of age]); SpO<sub>2</sub> measured in room air  $< 93\%$ ; high-flow nasal cannula or mechanical ventilation (invasive or noninvasive), ICU admission for  $> 4$  hours and/or failure to respond/unconscious. Secondary efficacy endpoints included hospitalizations due to RSV.

The VE results met the statistical criterion for success (a CI lower bound  $> 20\%$ ) for reducing severe LRTD due to RSV, at all timepoints to within 180 days. The VE results did not meet the statistical criterion for success (a CI lower bound  $> 20\%$ ) for reducing LRTD due to RSV; however, clinically meaningful efficacy was observed after 90 days through 180 days after birth.

Vaccine efficacy information is presented in Tables 6 to 10.

**Table 6 Vaccine Efficacy of ABRYSVO Against Severe LRTD Caused by RSV – Infants From Birth Through 6 Months of Age by Active Immunization of Pregnant Individuals (Study 1)<sup>a</sup>**

Time Period	ABRYSVO Number of Cases N=3,495 <sup>b</sup>	PLACEBO Number of Cases N=3,480 <sup>b</sup>	VE (%) (CI) <sup>c</sup>
90 days	6	33	81.8 (40.6, 96.3)
120 days	12	46	73.9 (45.6, 88.8)
150 days	16	55	70.9 (44.5, 85.9)
180 days	19	62	69.4 (44.3, 84.1)

CI=confidence interval; N=number of participants; RSV=respiratory syncytial virus; VE=vaccine efficacy

<sup>a</sup> The pre-specified success criterion was met for this endpoint evaluation.

<sup>b</sup> Evaluable efficacy population.

<sup>c</sup> 99.5% CI at 90 days; 97.58% CI at later intervals.

**Table 7 Vaccine Efficacy of ABRYSVO Against LRTD Caused by RSV – Infants From Birth Through 6 Months of Age by Active Immunization of Pregnant Individuals (Study 1)<sup>a</sup>**

Time Period	ABRYSVO Number of Cases N=3,495 <sup>b</sup>	PLACEBO Number of Cases N=3,480 <sup>b</sup>	VE (%) (CI) <sup>c</sup>
90 days	24	56	57.1 (14.7, 79.8)
120 days	35	81	56.8 (31.2, 73.5)
150 days	47	99	52.5 (28.7, 68.9)
180 days	57	117	51.3 (29.4, 66.8)

CI=confidence interval; N=number of participants; RSV=respiratory syncytial virus; VE=vaccine efficacy

<sup>a</sup> The pre-specified success criterion (a CI lower bound >20%) was not met for this endpoint evaluation at 90 days.

<sup>b</sup> Evaluable efficacy population.

<sup>c</sup> 99.5% CI at 90 days; 97.58% CI at later intervals.

**Table 8 Vaccine Efficacy of ABRYSVO Against Severe LRTD Caused by RSV – Infants From Birth Through 6 Months of Age by Active Immunization of Pregnant Individuals at 32 Through 36 Weeks Gestational Age (Study 1)<sup>a</sup>**

Time Period	ABRYSVO Number of Cases N=1572 <sup>b</sup>	PLACEBO Number of Cases N=1539 <sup>b</sup>	VE (%) (CI) <sup>c</sup>
90 days	1	11	91.1 (38.8, 99.8)
180 days	6	25	76.5 (41.3, 92.1)

CI=confidence interval; N=number of participants; n=number of cases; RSV=respiratory syncytial virus; VE=vaccine efficacy

<sup>a</sup> This descriptive subgroup analysis was not controlled for multiple comparisons; results from 90 days and 180 days are presented.

<sup>b</sup> Evaluable efficacy population.

<sup>c</sup> 95% CI.



**Table 9 Vaccine Efficacy of ABRYSVO Against LRTD Caused by RSV – Infants From Birth Through 6 Months of Age by Active Immunization of Pregnant Individuals at 32 Through 36 Weeks Gestational Age (Study 1)<sup>a</sup>**

Time Period	ABRYSVO Number of Cases N=1572 <sup>b</sup>	PLACEBO Number of Cases N=1539 <sup>b</sup>	VE (%) (CI) <sup>c</sup>
90 days	14	21	34.7 (-34.6, 69.3)
180 days	24	55	57.3 (29.8, 74.7)

CI=confidence interval; N=number of participants; n=number of cases; RSV=respiratory syncytial virus;

VE=vaccine efficacy

<sup>a</sup> This descriptive subgroup analysis was not controlled for multiple comparisons; results from 90 days and 180 days are presented.

<sup>b</sup> Evaluable efficacy population.

<sup>c</sup> 95% CI.

**Table 10 Vaccine Efficacy of ABRYSVO Against Hospitalization Due to RSV – Infants From Birth Through 6 Months of Age by Active Immunization of Pregnant Individuals (Study 1)<sup>a</sup>**

Time Period	ABRYSVO Number of Cases N=3,495 <sup>b</sup>	PLACEBO Number of Cases N=3,480 <sup>b</sup>	VE (%) (CI) <sup>c</sup>
90 days	10	31	67.7 (15.9, 89.5)
120 days	15	37	59.5 (8.3, 83.7)
150 days	17	39	56.4 (5.2, 81.5)
180 days	19	44	56.8 (10.1, 80.7)

CI=confidence interval; N=number of participants; n=number of cases; RSV=respiratory syncytial virus;

VE=vaccine efficacy

<sup>a</sup> NCT04424316.

<sup>b</sup> Evaluable efficacy population

<sup>c</sup> 99.17% CI.

## 12.2 Efficacy in Individuals 60 Years of Age and Older

Study 3 (NCT05035212) is an ongoing Phase 3, multicenter, randomized, double-blind, placebo-controlled study to assess the efficacy and safety of ABRYSVO in the prevention of RSV-associated lower respiratory tract disease in individuals 60 years of age and older. Participants are planned to be followed for up to two RSV seasons, approximately 25 months.

Participants were randomized (1:1) to receive ABRYSVO (n=17,197) or placebo (n=17,186). Randomization was stratified by age, 60-69 years (n=21,499, 63%), 70-79 years (n=10,948, 32%), and ≥80 years (n=1,934, 6%). Healthy adults and adults with stable chronic diseases were included. Among enrolled participants 15% had stable chronic cardiopulmonary conditions such as chronic obstructive pulmonary disease (COPD), asthma, or congestive heart failure (CHF).

Starting 14 days after study vaccination (study Day 15), all participants were actively monitored for onset of acute respiratory illness (ARI) symptoms: new or increased sore throat, nasal congestion, nasal discharge, cough, wheezing, sputum production, or shortness of breath. If the participant experienced 1 or more ARI symptoms, a mid-turbinate nasal swab was collected within 7 days of onset of symptoms and tested by reverse transcriptase polymerase chain reaction (RT-PCR) for RSV.

RSV-associated lower respiratory tract disease (RSV-LRTD) was evaluated in Study 3. A case of RSV-LRTD was defined as an RT-PCR confirmed RSV illness with two or more, or three or more, of the following respiratory symptoms within 7 days of symptom onset and lasting more than 1 day during the same illness: new or increased cough, wheezing, sputum production, shortness of breath, or tachypnea ( $\geq 25$  breaths/min or 15% increase from resting baseline). A case of RSV-associated severe lower respiratory tract disease was defined as a case meeting the RSV-LRTD criteria plus at least one of the following: hospitalization due to RSV-LRTD, new or increased oxygen supplementation, or mechanical ventilation including Continuous Positive Airway Pressure (CPAP).

#### Efficacy against Respiratory Syncytial Virus-associated Lower Respiratory Tract Disease in Individuals 60 Years of Age and Older

Vaccine efficacy (VE), against RSV-LRTD, defined as the relative risk reduction of first episode of RSV-LRTD in the ABRYSVO group compared to the placebo group in the first RSV season, was assessed.

The study met the pre-specified success criteria for demonstration of efficacy of ABRYSVO for the primary objectives of prevention of RSV-LRTD with  $\geq 2$  symptoms and prevention of RSV-LRTD with  $\geq 3$  symptoms. The median duration of follow-up for efficacy was 7 months.

Vaccine efficacy information is presented in Table 11.

**Table 11 Vaccine Efficacy of ABRYSVO Against RSV-LRTD – Individuals 60 years of Age and Older (Study 3)<sup>a</sup>**

<b>Efficacy Endpoint</b>	<b>ABRYSVO N=16,306<sup>b</sup> n</b>	<b>Placebo N=16,308<sup>b</sup> n</b>	<b>VE (%) (96.66% CI)</b>
First episode of RSV-associated lower respiratory tract disease with $\geq 2$ symptoms	11	33	66.7 (28.8, 85.8)
First episode of RSV-associated lower respiratory tract disease with $\geq 3$ symptoms	2	14	85.7 (32.0, 98.7)

CI=confidence interval; N=number of participants; n=number of cases; RSV=respiratory syncytial virus; VE=vaccine efficacy (VE based on case count ratio is calculated as  $1-(P/[1-P])$ , where P is the number of RSV preF cases divided by the total number of cases)

<sup>a</sup> NCT05035212.

<sup>b</sup> Evaluable efficacy population.

There were 2 cases of RSV-associated severe lower respiratory tract disease in the placebo group and no cases in the ABRYSVO group.

### **12.3 Concomitant Vaccine Administration with Tetanus Toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis Vaccine, Adsorbed**

Study 4 (NCT04071158) was a Phase 2, placebo-controlled, randomized, observer-blind study to evaluate the safety, tolerability, and immunogenicity of ABRYSVO (at dose levels

120 µg and 240 µg, with or without Al(OH)<sub>3</sub>) when administered concomitantly with Tdap in non-pregnant women 18 through 49 years of age.

Antibody responses to antigens contained in ABRYSV0 and Tdap were assessed 1 month after vaccination in a population of non-pregnant adult individuals. Lower geometric mean antibody concentrations (GMCs) to the acellular pertussis antigens (pertussis toxin [PT], filamentous hemagglutinin [FHA], and pertactin [PRN]) were observed when ABRYSV0 was administered concomitantly with a tetanus, diphtheria and acellular pertussis vaccine (Tdap) compared to pertussis GMCs when Tdap was administered alone. The lower limit (LL) of the 2-sided 95% confidence interval of the GMC ratio ( $GMC_{ABRYSV0+Tdap}/GMC_{Tdap}$ ) was 0.64 for PT, 0.50 for FHA, and 0.48 for PRN, which did not meet the pre-specified non-inferiority criterion (lower limit of the 95% confidence interval for the GMC ratio is >0.67). The clinical relevance of this finding is unknown. The non-inferiority criteria for tetanus, diphtheria and RSV vaccine antigens were met [see *Drug Interactions* (8)].

## 13 HOW SUPPLIED/STORAGE AND HANDLING

### 13.1 How Supplied

#### Powder

Powder for 1 dose in a vial (type 1 glass or equivalent) with a stopper (synthetic chlorobutyl rubber) and a flip off cap.

#### Solvent

Solvent for 1 dose in a pre-filled syringe (type 1 glass) with a stopper (synthetic chlorobutyl rubber) and a tip cap (synthetic isoprene/bromobutyl blend rubber).

#### Vial adaptor

Sterile vial adaptor.

#### Pack size

Pack containing 1 vial (antigens) of powder, 1 pre-filled syringe of solvent, 1 vial adaptor with 1 needle or without needles.

Pack containing 5 vials of powder (antigens), 5 pre-filled syringes of solvent, 5 vial adaptors with 5 needles or without needles.

Pack containing 10 vials of powder (antigens), 10 pre-filled syringes of solvent, 10 vial adaptors with 10 needles or without needles.

Not all presentations may be available locally.

## **13.2 Storage and Handling**

### **Storage Before Reconstitution**

Store refrigerated at 2°C to 8°C in the original carton. Do not freeze. Discard if the carton has been frozen.

### **Storage After Reconstitution**

After reconstitution, administer ABRYSV0 immediately or store at room temperature (15°C to 30°C) and use within 4 hours. Do not store reconstituted vaccine under refrigerated conditions (2°C to 8°C). Do not freeze reconstituted vaccine.

## **14 PATIENT COUNSELING INFORMATION**

Prior to administration of this vaccine:

- Inform vaccine recipient of the potential benefits and risks of vaccination with ABRYSV0.

## **15 PRODUCT OWNER**

Pfizer Inc.  
New York,  
United States

RSV-SIN-0923/3

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