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U.S. FOOD & DRUG ADMINISTRATION

Vaccines and Related Biological Products
Advisory Committee Meeting
February 28, 2023

FDA Review of Efficacy and Safety of ABRYSVO (RSVpreF) Biologics Licensing Application

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Division of Vaccines and Related Products Applications

Outline

- Introduction
- Overview of Clinical Studies
- Efficacy Data
- Safety Data
- Pharmacovigilance Plan
- Summary and Voting Questions for VRBPAC

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ABRYSVO – RSVpreF

Vaccine composition	RSV recombinant stabilized prefusion F (preF) protein subunit vaccine • 60 µg RSVpreF from RSV A • 60 µg RSVpreF from RSV B
Dosing regimen	A single 0.5 mL (120 µg) dose administered intramuscularly
Applicant's proposed indication	Prevention of acute respiratory disease and lower respiratory tract disease caused by respiratory syncytial virus (RSV) in individuals 60 years of age and older by active immunization.

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Clinical Studies

Shaded in grey=not to be discussed today

Study	Country	Description	Population	Study Groups	
				RSVpreF	Placebo
C3671013 *(Ongoing)* Phase 3	**US, Canada, Finland, Japan, The Netherlands, South Africa, Argentina**	**Efficacy** **Safety** and **Immunogenicity**	**Adults ≥ 60 years**	**17,215**	**17,069**
C3671014 Phase 3	US	Lot-to-Lot Safety and Immunogenicity	Adults 18-49 years	745	247
Four additional Phase 1 and Phase 2 studies	US, UK, Australia	Safety and Immunogenicity Dose-finding, with/without $Al(OH)_3$+CpG or $Al(OH)_3$ alone Concomitant administration	Age range: 18-85 years	1,982	343

Study 1013 Design

Ongoing Phase 3 Efficacy and Safety Study

- Total of 34,284 participants ≥60 years of age
- Study groups: RSVpreF or placebo (randomized 1:1), IM injection
- Primary efficacy assessed during first RSV season
- Study to be conducted over 2 RSV seasons

- Randomization stratified by age: 60-69 years, 70-79 years, ≥80 years
- Enrolled healthy adults and adults with stable chronic diseases
- Participants were actively monitored for acute respiratory illness (ARI) and lower respiratory tract illness (LRTI) symptoms starting 14 days after study vaccination
- Safety monitoring:
  - Subset of participants: solicited local and systemic adverse reactions (7 days).
  - All participants: unsolicited adverse events (AEs) through 1 month; newly diagnosed chronic medical conditions (NDCMCs) and serious adverse events (SAEs) through the entire study.

Study 1013 Timeline

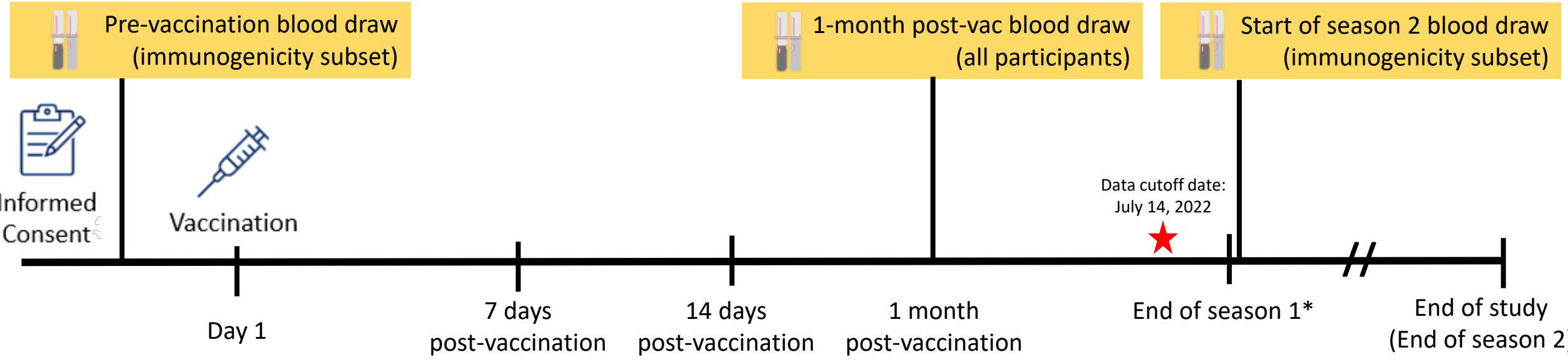
SAE, NDCMC monitoring

Unsolicited AE monitoring

Reactogenicity subset

Solicited local and systemic reactions

Active surveillance for ARI and LRTI symptoms



*=For the 32,614 participants included in the evaluable efficacy population, 66.3% (n=21617) have completed season 1 surveillance at the time of the data cutoff

Case Definitions, Study 1013

ARI is defined as ≥1 of the following: sore throat, nasal congestion, nasal discharge, wheezing, sputum production, cough, shortness of breath

LRTI-RSV with ≥2 or ≥3 Symptoms

ARI with ≥2 or ≥3 of the following LRTI signs/symptoms lasting more than 1 day during the same illness:

- Wheezing
- Sputum production
- Cough
- Shortness of breath
- Tachypnea (≥25 breaths/min or ≥15% increase from resting baseline)

AND RT-PCR-confirmed RSV infection within 7 days of ARI symptom onset

Study 1013: Primary Efficacy Endpoint and Objectives

Primary endpoint

Efficacy objective: To demonstrate the vaccine efficacy (VE) of RSVpreF in preventing LRTI-RSV, starting 14 days after vaccination, in the 1st RSV season.
1st primary endpoint: VE against LRTI-RSV with ≥2 symptoms
2nd primary endpoint : VE against LRTI-RSV with ≥3 symptoms
Assessed sequentially as ordered

VE is defined as 1 - Risk Ratio (RR)

The primary objective would be met if the lower bound of the CI for VE for LRTI-RSV with ≥2 symptoms is >20% at either the interim or primary analysis
(based on the Pocock-adjusted CI at interim analysis or primary analysis)

Interim analysis (IA) planned after accrual of ≥ 29 LRTI-RSV cases with ≥ 2 symptoms

IA conducted upon accrual of 44 cases (data cutoff: July 8, 2022)

Primary analysis planned after accrual of ≥59 LRTI-RSV cases with ≥ 2 symptoms

Primary analysis only occurs if the primary objective not met at IA

Secondary Efficacy Endpoints

To demonstrate the efficacy of RSVpreF in preventing severe LRTI-RSV (sLRTI-RSV)	VE against first-episode sLRTI-RSV cases, starting 14 days after study vaccination.

sLRTI-RSV defined as meeting LRTI-RSV criteria **plus** at least 1 of the following:

- Hospitalization due to LRTI-RSV
- New/increased oxygen supplementation
- New/increased mechanical ventilation, including CPAP

To describe the efficacy of RSVpreF in preventing ARI-RSV	VE against first-episode ARI-RSV cases, starting 14 days after study vaccination.

Additional Planned Analyses

All participants remain in blinded follow-up

Planned secondary and exploratory objectives:

- VE in prevention of LRTI-RSV, ARI-RSV, and sLRTI-RSV across 1 and 2 RSV seasons
- Immunogenicity
- Rates and descriptions of LRTI-associated healthcare resource utilization

Study 1013 Analysis Populations

Population	Description
Safety Population	All enrolled participants who received the study intervention.
Modified Intent-to-Treat (mITT) Efficacy Population	All participants who were randomized and received study intervention.
Evaluable Efficacy Population	All study participants who met the following criteria: • Were eligible for the study. • Received study intervention to which they were randomized • Follow-up through 14 days post-vaccination • Had no major protocol violations before the symptom onset date of the confirmed ARI or LRTI case.
eDiary Subset Safety Population	All participants included in the Reactogenicity Subset who received the study intervention and with at least 1 day of eDiary data transferred.

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Study 1013: Participant Disposition

Population	RSVpreF N=17197 n (%)	Placebo N=17186 n (%)
Randomized Set	17197 (100.0)	17186 (100.0)
Modified Intent-To-Treat (mITT) Efficacy Population	16999 (98.8)	16988 (98.8)
Evaluable Efficacy Population	16306 (94.8)	16308 (94.9)
Excluded from the Evaluable Efficacy Population	891 (5.2)	878 (5.1)
Reason for exclusion	--	--
Not eligible for this study	42 (0.2)	41 (0.2)
Did not receive study vaccine	49 (0.3)	50 (0.3)
Received study vaccine but not as randomized	112 (0.7)	110 (0.6)
Received multiple vaccinations due to multiple enrollments at different sites	109 (0.6)	104 (0.6)
Efficacy surveillance duration was less than 15 days (<14 days after vaccination)	693 (4.0)	687 (4.0)
≥1 Important protocol deviation prior to symptom onset date of confirmed ARI-RSV case	72 (0.4)	68 (0.4)

Study 1013: Demographics, Evaluable Efficacy Population

Characteristic	RSVpreF N=16306 n (%)	Placebo N=16308 n (%)
Sex	--	--
Male	8327 (51.1)	8225 (50.4)
Female	7979 (48.9)	8083 (49.6)
Age, years	--	--
60-69 years	10176 (62.4)	10191 (62.5)
70-79 years	5207 (31.9)	5196 (31.9)
≥80 years	923 (5.7)	921 (5.6)
Country	--	--
USA	10093 (61.9)	10097 (61.9)
Argentina	3041 (18.6)	3042 (18.7)
Japan	1151 (7.1)	1153 (7.1)
The Netherlands	660 (4.0)	654 (4.0)
Canada	509 (3.1)	505 (3.1)
South Africa	467 (2.9)	469 (2.9)
Finland	385 (2.4)	388 (2.4)

Study 1013: Demographics, Evaluable Efficacy Population (continued)

Characteristic	RSVpreF N=16306 n (%)	Placebo N=16308 n (%)
Race	--	--
African American/Black	2131 (13.1)	2162 (13.3)
American Indian or Alaska Native	44 (0.3)	34 (0.2)
Asian	1341 (8.2)	1330 (8.2)
Native Hawaiian or other Pacific Islander	10 (<0.1)	15 (<0.1)
White	12654 (77.6)	12652 (77.6)
Multiracial	44 (0.3)	36 (0.2)
Ethnicity	--	--
Hispanic/Latino	5603 (34.4)	5601 (34.3)
Not Hispanic/Latino	10614 (65.1)	10616 (65.1)

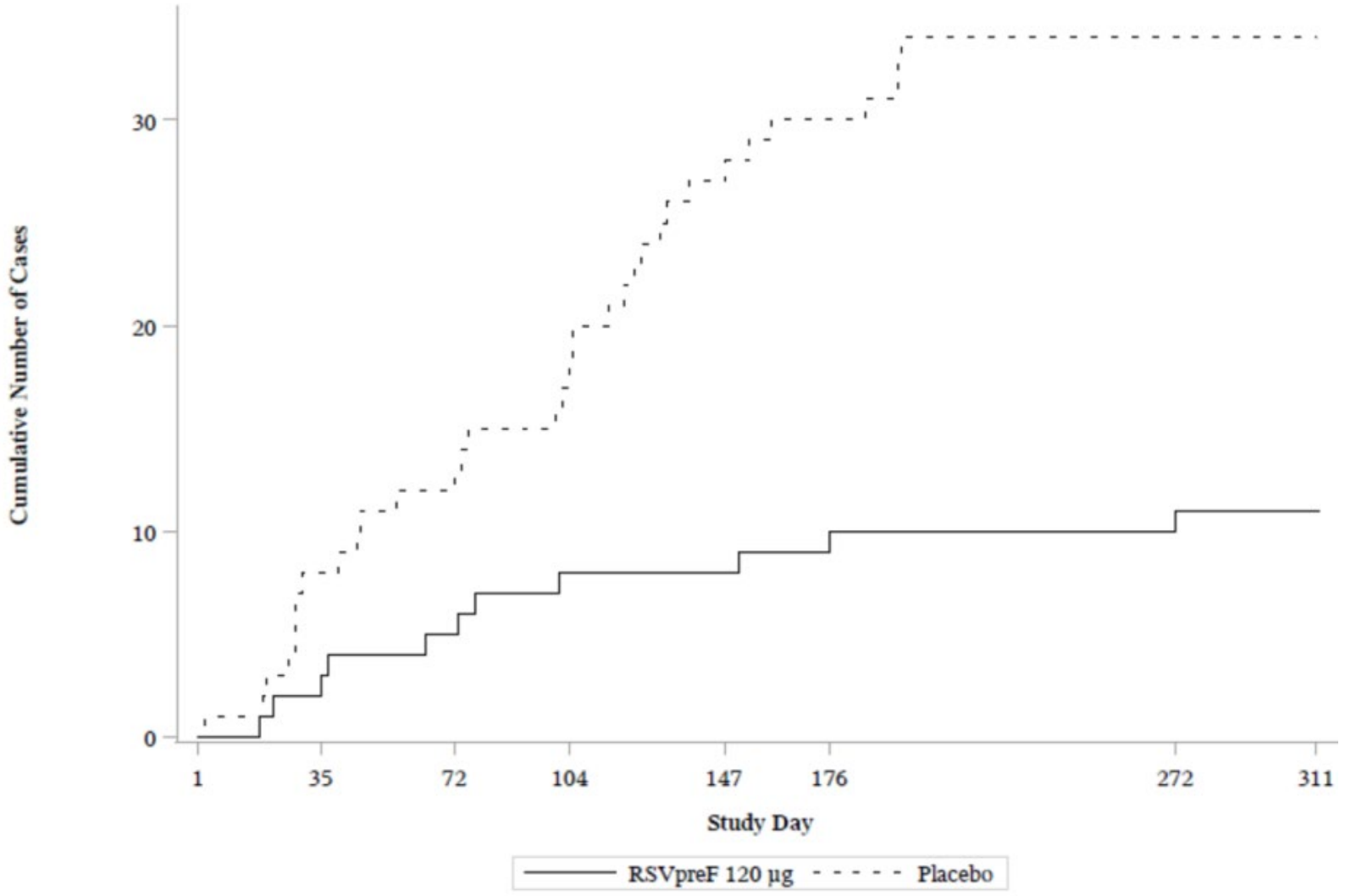
Study 1013: Baseline At-Risk Conditions, Evaluable Efficacy Population

Prespecified At-Risk Condition	RSVpreF N=16306 n (%)	Placebo N=16308 n (%)
With ≥1 prespecified significant condition	8314 (51.0)	8396 (51.5)
Current tobacco use	2450 (15.0)	2432 (14.9)
Diabetes	3034 (18.6)	3147 (19.3)
Lung disease	1827 (11.2)	1916 (11.7)
Heart disease	2093 (12.8)	2120 (13.0)
Liver disease	290 (1.8)	299 (1.8)
Renal disease	470 (2.9)	436 (2.7)
With ≥1 chronic cardiopulmonary condition	2420 (14.8)	2498 (15.3)
Asthma	1452 (8.9)	1446 (8.9)
Chronic obstructive pulmonary disease (COPD)	918 (5.6)	991 (6.1)
Congestive heart failure (CHF)	281 (1.7)	296 (1.8)

Study 1013: Primary Efficacy Endpoints
VE Against LRTI-RSV With ≥2 or ≥3 Symptoms

Efficacy Endpoint	RSVpreF N=16306 Cases n (%) Incidence Rate per 1000 Person-Years	Placebo N=16308 Cases n (%) Incidence Rate per 1000 Person-Years	VE, % (96.66% CI)
First episode of LRTI-RSV with ≥2 symptoms	11 (0.1) 1.2	33 (0.2) 3.6	66.7 (28.8, 85.8)
First episode of LRTI-RSV with ≥3 symptoms	2 (<0.1) 0.2	14 (0.1) 1.5	85.7 (32.0, 98.7)

Study 1013: Cumulative Case Accrual Curve From Day of Vaccination, LRTI-RSV ≥2 symptoms, mITT Efficacy Population



Cumulative Number of Events

RSVpreF 120 µg	0	3	5	8	8	10	11	11
Placebo	0	8	13	18	28	30	34	34

Study 1013: VE Against LRTI-RSV With ≥2 Symptoms
Subgroup Analyses- Age

Subgroup	RSVpreF		Placebo		VE, % (96.66% CI)
Age at vaccination	**n**	**N**	**n**	**N**	**--**
60-69 years	8	10,176	19	10,191	57.9 (-7.4, 85.3)
70-79 years	2	5,207	9	5,196	77.8 (-18.7, 98.1)
≥80 years	1	923	5	921	80.0 (-104.3, 99.7)

Study 1013: VE Against LRTI-RSV With ≥2 Symptoms
Subgroup Analyses- Predefined Conditions

Subgroup	RSVpreF		Placebo		VE, % (96.66% CI)
Prespecified Significant Condition	**n**	**N**	**n**	**N**	**--**
With no prespecified significant condition	5	7,992	17	7,912	70.6 (10.7, 92.4)
With ≥1 prespecified significant condition	6	8,314	16	8,396	62.5 (-8.4, 89.1)
With ≥1 chronic cardiopulmonary condition	4	2,420	6	2,498	33.3 (-213.7, 87.9)

Study 1013: VE Against LRTI-RSV With ≥2 or ≥3 Symptoms, by RSV Subgroup, Evaluable Efficacy Population

Endpoint	RSVpreF N=16306 Cases n (%); Incidence Rate per 1000 Person-Years	Placebo N=16308 Cases n (%); Incidence Rate per 1000 Person-Years	VE, % (96.66 CI)
First episode of LRTI-RSV with ≥2 symptoms	--	--	--
RSV Subgroup A	1 (<0.1); 0.1	9 (0.1); 1.0	88.9 (10.6, 99.8)
RSV Subgroup B	10 (0.1); 1.1	23 (0.1); 2.5	56.5 (-0.7, 82.8)
First episode of LRTI-RSV with ≥3 symptoms	--	--	--
RSV Subgroup A	1 (<0.1); 0.1	3 (<0.1); 0.3	66.7 (-393.7, 99.6)
RSV Subgroup B	1 (<0.1); 0.1	10 (0.1); 1.1	90.0 (21.8, 99.8)

Study 1013: Post-hoc analyses*
VE Against Medically Attended LRTI-RSV With ≥2 and ≥3 Symptoms

Endpoint	RSVpreF N=16306 Cases n (%) Incidence Rate per 1000 Person-Years	Placebo N=16308 Cases n (%) Incidence Rate per 1000 Person-Years	VE, % (95% CI)
Medically attended LRTI-RSV with ≥2 symptoms	7 (<0.1) 0.8	20 (0.1) 2.2	65.1 (14.0, 87.5)
Medically attended LRTI-RSV with ≥3 symptoms	2 (<0.1) 0.2	10 (0.1) 1.1	80.0 (6.3, 97.9)

**FDA requested analyses*

A **medically attended LRTI-RSV case** was defined as an episode with any outpatient or inpatient visit, not including illness visits to the study site.

Study 1013: Severe LRTI-RSV

Definition

sLRTI-RSV defined as meeting LRTI-RSV criteria **plus** at least 1 of the following:

- Hospitalization due to LRTI-RSV
- New/increased oxygen supplementation
- New/increased mechanical ventilation, including CPAP

Cases

Two cases of sLRTI: Both **placebo recipients**

- 66 M, with history of obesity; positive for RSV B, hospitalized and required supplemental oxygen
- 63 F, with history of asthma; positive for RSV B, hospitalized

Formal evaluation of endpoint not performed due to insufficient number of sLRTI-RSV cases accrued by data cutoff

Study 1013: Preliminary Estimate of VE Against ARI-RSV

Endpoint	RSVpreF N=16306 Cases n (%) Incidence Rate per 1000 Person-Years	Placebo N=16308 Cases n (%) Incidence Rate per 1000 Person-Years	VE, % (95% CI)
First episode of ARI-RSV	22 (0.1) 2.4	58 (0.4) 6.3	62.1 (37.1, 77.9)

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Study 1013: Demographic and Baseline Characteristics, Safety Population

Characteristic	RSVpreF N=17215 n (%)	Placebo N=17069 n (%)
Sex	--	--
Male	8800 (51.1)	8601(50.4)
Female	8415 (48.9)	8468 (49.6)
Age, years	--	--
60-69 years	10756 (62.5)	10680 (62.6)
70-79 years	5488 (31.9)	5431 (31.8)
≥80 years	970 (5.6)	958 (5.6)
Country	--	--
United States	10319 (59.9)	10182 (59.7)
Argentina	3660 (21.3)	3657 (21.4)
Japan	1159 (6.7)	1156 (6.8)
The Netherlands	687 (4.0)	681 (4.0)
Canada	509 (3.0)	506 (3.0)
South Africa	495 (2.9)	497 (2.9)
Finland	386 (2.2)	390 (2.3)

Study 1013: Demographic and Baseline Characteristics, Safety Population (continued)

Characteristic	RSVpreF N=17215 n (%)	Placebo N=17069 n (%)
Race	--	--
African American/Black	2206 (12.8)	2207 (12.9)
American Indian or Alaska Native	44 (0.3)	36 (0.2)
Asian	1352 (7.9)	1333 (7.8)
Native Hawaiian or other Pacific Islander	10 (<0.1)	15 (<0.1)
White	13475 (78.3)	13360 (78.3)
Ethnicity	--	--
Hispanic/Latino	6384 (37.1)	6260 (36.7)
Not Hispanic/Latino	10740 (62.4)	10715 (62.8)

Study 1013: Disposition, Safety Population

Population	RSVpreF N=17215 n (%)	Placebo N=17069 n (%)
Completed 6 months safety follow-up	13273 (77.1)	13122 (76.9)
Participants withdrawn after vaccination	869 (5.0)	941 (5.5)
Reactogenicity subset	3820 (22.2)	3708 (21.7)
eDiary subset safety population	3630 (95.0)[a]	3539 (95.4)[a]

[a]percent based on reactogenicity subset

Study 1013: Proportion of Participants Reporting at Least One Adverse Event Following Vaccination

AE Type: Monitoring Period	RSVpreF N=17215 n (%)	Placebo N=17069 n (%
Immediate: 30 minutes	35 (0.2)	31 (0.2)
Unsolicited: Through the 1-month follow-up visit	1537 (8.9)	1451 (8.5)
Related unsolicited AEs	230 (1.3)	159 (0.9)
Severe unsolicited AEs	65 (0.4)	51 (0.3)
Life-threatening unsolicited AEs	24 (0.1)	19 (0.1)
Newly diagnosed chronic medical condition: Entire study period	301 (1.7)	313 (1.8)
AEs leading to study withdrawal: Entire study period	10 (<0.1)	6 (<0.1)
SAEs: Entire study period	396 (2.3)	387 (2.3)
Related SAEs	3 (<0.1)	0 (0)
Deaths: Entire study period	52 (0.3)	49 (0.3)

Study 1013: Solicited Local Reactions

Solicited Adverse Reaction	RSVpreF N=3619-3621 n (%)	Placebo N=3532-3539 n (%)
Local reaction ≥ Grade 1	441 (12.2)	235 (6.6)
Grade 3	8 (0.2)	2 (<0.1)
Pain[a]	--	--
≥ Grade 1	385 (10.6)	212 (6.0)
Grade 3	2 (<0.1)	(0)
Erythema[b]	--	--
≥ Grade 1	97 (2.7)	23 (0.7)
Grade 3	4 (0.1)	(0)
Swelling[b]	--	--
≥ Grade 1	89 (2.5)	16 (0.5)
Grade 3	4 (0.1)	2 (<0.1)

a. Grade 1: does not interfere with activity; grade 2: interferes with activity; grade 3: prevents daily activity
b. Grade 1: 2.5 cm to 5.0 cm; Grade 2: >5.0 cm to 10.0 cm; Grade 3: >10.0 cm

Study 1013: Solicited Systemic Reactions

Solicited Adverse Reaction	RSVpreF N=3619-3621 n (%)	Placebo N=3532-3539 n (%)
Systemic reaction ≥ Grade 1	994 (27.5)	909 (25.7)
Grade 3	27 (0.7)	20 (0.6)
Grade 4 (fever >40.0°C)	(0)	1 (<0.1)
Fatigue[a]	--	--
≥ Grade 1	562 (15.5)	508 (14.4)
Grade 3	12 (0.3)	5 (0.1)
Headache[a]	--	--
≥ Grade 1	465 (12.8)	415 (11.7)
Grade 3	4 (0.1)	3 (<0.1)
Muscle Pain[a]	--	--
≥ Grade 1	367 (10.1)	297 (8.4)
Grade 3	8 (0.2)	3 (<0.1)
Joint Pain[a]	--	--
≥ Grade 1	272 (7.5)	244 (6.9)
Grade 3	3 (<0.1)	2 (<0.1)

a. grade 1: does not interfere with activity; grade 2: some interference with activity; grade 3: prevents daily routine activity.

Study 1013: Solicited Systemic Reactions (continued)

Solicited Adverse Reaction	RSVpreF N=3619-3621 n (%)	Placebo N=3532-3539 n (%)
Nausea[a]	--	--
≥ Grade 1	124 (3.4)	132 (3.7)
Grade 3	0 (0)	3 (<0.1)
Vomiting[b]	--	--
≥ Grade 1	32 (0.9)	30 (0.8)
Grade 3	0 (0)	2 (<0.1)
Diarrhea[c]	--	--
≥ Grade 1	214 (5.9)	183 (5.2)
Grade 3	4 (0.1)	4 (0.1)
Fever (temperature ≥38°C)	--	--
Any Fever	52 (1.4)	51 (1.4)
≥38.0-38.4°C	23 (0.6)	27 (0.8)
>38.4-38.9°C	28 (0.8)	21 (0.6)
>38.9-40.0°C	1 (<0.1)	2 (<0.1)
>40.0°C	0 (0)	1 (<0.1)

a. grade 1: does not interfere with activity; grade 2: some interference with activity; grade 3: prevents daily routine activity.
b. grade 1: 1 to 2 times in 24 hours; grade 2: >2 times in 24 hours; grade 3: requires intravenous hydration.
c. grade 1: 2 to 3 loose stools in 24 hours; grade 2: 4 to 5 loose stools in 24 hours; grade 3: 6 or more loose stools in 24 hours.

Unsolicited Adverse Events (1 month)

- Overall, AEs were reported at similar rates between the RSVpreF (9.0%) and placebo (8.5%) groups. Most common (>1%) by MedDRA System Organ Class (SOC):
  - *Infection and Infestations*
  - *Respiratory, thoracic and mediastinal disorders*
  - *General disorders and administration site conditions*

- Numerical imbalance noted in events of **atrial fibrillation** through 1 month: RSVpreF group=10 vs. placebo group=4
  - Medical history of atrial fibrillation: RSVpreF group: 6/10, placebo group: 2/4
  - Onset: 18 to 30 days post-vaccination
  - None of these events were fatal
  - None assessed as related by investigator
  - **FDA review of these cases is ongoing**

Serious Adverse Events/Deaths

SAEs reported at similar rate in the 2 groups (2.3% in each group)

SAEs considered possibly related by investigator and FDA

Three events, all in RSVpreF group

- ***Hypersensitivity***
  61 yo F, symptoms 8 hours post-vaccination, hospitalized, diagnosis: allergic drug reaction, resolved by 5 days
- ***Guillain-Barre Syndrome***
  66 yo M, symptoms 7 days post-vaccination, hospitalized, resolving as of data cutoff
- ***Miller Fisher Syndrome***
  66 yo F with DM-2, symptoms 8 days post-vaccination; hospitalized, MFS diagnosis by neurology, resolved by 3 months

Deaths through data cutoff: 0.3% in RSVpreF group and 0.3% in placebo group

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Pharmacovigilance Plan

The Applicant will conduct passive and active surveillance activities for continued vaccine safety monitoring, including routine pharmacovigilance.

Missing information	Immunocompromised older adults
Surveillance Activities	• Planned postmarketing safety study in immunocompromised older adults

Important Potential Risks	• GBS and other immune-mediated demyelinating conditions • Cardiac disorders
Surveillance Activities	• Expedited reporting for all cases of GBS and other immune-mediated demyelinating conditions and Cardiac disorders • Aggregate analysis of GBS and other immune-mediated demyelinating conditions and Cardiac disorders in periodic safety reports • Planned postmarketing safety study to assess the risk of GBS and other immune-mediated demyelinating conditions among individuals vaccinated with ABRYSVO (RSVpreF)

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Summary - Efficacy

- VE to prevent first-episode LRTI-RSV with ≥2 and ≥3 symptoms were 66.7% (96.66% CI 28.8, 85.8) and 85.7% (96.66% CI 32.0, 98.7), respectively
  - Study success criterion met
- Descriptive point estimates for VE against LRTI-RSV appear preserved among participants ≥80 years and among participants with at least one at-risk condition, but were limited by small subpopulation sizes
- Preliminary VE against ARI-RSV was 62.1% (95% CI 37.1, 77.9)
- Data are not currently available on:
  - Duration of vaccine effectiveness
  - VE in immunocompromised and frail elderly individuals
  - VE in preventing severe LRTI cases
  - Data regarding concomitant administration with vaccines routinely recommended for use in this population

Summary - Safety

- Study included 34,284 participants (17,215 who received RSVpreF), of which 26,395 participants (77.0%) have had at least 6 months of follow-up
- Solicited local and systemic reactions were generally mild to moderate and of short duration
- Within 1 month after vaccination, a numerical imbalance was observed for events of atrial fibrillation (10 in RSVpreF group vs 4 in placebo group). FDA review of these events is ongoing.
- Serious adverse events were balanced between the RSVpreF and placebo groups (2.3% in both groups)
- Three SAEs (hypersensitivity, GBS, and Miller Fisher Syndrome) were assessed by FDA as possibly related to RSVpreF, in agreement with the Investigator's assessment
- Review of safety data from the 5 supportive clinical studies (~1,200 participants who received RSVpreF final formulation) did not reveal any other cases of GBS or other immune-mediate demyelinating condition post-vaccination, or any other safety signal

Voting Questions for VRBPAC

1. Are the available data adequate to support the safety of ABRYSVO (RSVpreF) when administered to individuals 60 years of age and older for the prevention of lower respiratory tract disease caused by RSV?
   Please vote "Yes" or "No"
2. Are the available data adequate to support the effectiveness of ABRYSVO (RSVpreF) for the prevention of lower respiratory tract disease caused by RSV in individuals 60 years of age and older?
   Please vote "Yes" or "No"

Supplemental Slides

Study 1013: Efficacy

Vaccine Efficacy of RSVpreF Against First Episode of LRTI-RSV With ≥2 Symptoms Starting 14 Days After Vaccination, By Subgroup, Evaluable Efficacy Population

Subgroup	RSVpreF Cases n/N (%)	Placebo Cases n/N (%)	VE, % (96.66% CI)
Sex	--	--	--
Male	6/8,327	17/8,225	64.7 (-0.6, 89.7)
Female	5/7,979	16/8,083	68.8 (3.9, 92.0)
Race	--	--	--
White	8/12,654	30/12,652	73.3 (36.9, 90.3)
Black or African American	3/2,131	2/2,162	-50.0 (-2143.8, 85.5)
Asian	0/1,341	1/1,330	100.0 (-5788.0, 100.0)
Ethnicity	--	--	--
Hispanic/Latino	1/5,603	7/5,601	85.7 (-25.1, 99.8)
Non-Hispanic/non-Latino	10/10,614	26/10,616	61.5 (12.8, 84.6)
Country	--	--	--
United States	7/10,093	19/10,097	63.2 (2.2, 88.0)
Canada	0/509	1/505	100.0 (-5788.0, 100.0)
The Netherlands	1/660	2/654	50.0 (-1105.6, 99.4)
South Africa	2/467	6/469	66.7 (-109.5, 97.4)
Argentina	1/3,041	5/3,042	80.0 (-104.3, 99.7)

Study 1013: Efficacy

Primary Endpoint Vaccine Efficacy of RSVpreF Against First Episode of LRTI-RSV With ≥3 Symptoms, by Age Subgroup and Predefined Conditions

Subgroup	RSVpreF Cases, n/N (%)	Placebo Cases, n/N (%)	VE, % (96.66% CI)
Age at vaccination	--	--	--
60-69 years	**2**/10,176 (0.02)	**9**/10,191 (0.09)	77.8 (-18.7, 98.1)
70-79 years	**0**/5,207 (0)	**2**/5,196 (0.04)	100 (-573.8, 100)
≥80 years	**0**/923 (0)	**3**/921 (0.33)	100 (-191.2, 100)
Prespecified Significant Condition	--	--	--
With no Prespecified Significant Condition	**0**/7,992 (0)	**6**/7,912 (0.08)	100 (2.2, 100)
With ≥1 Prespecified Significant Condition	**2**/8,314 (0.02)	**8**/8,396 (0.10)	75 (-39.1, 97.9)
With ≥1 chronic cardiopulmonary condition	**2**/2,420 (0.08)	**4**/2,498 (0.16)	50.0 (-302.1, 96.4)