TRUMENBA
Meningococcal group B vaccine

1. NAME OF THE MEDICINAL PRODUCT

Trumenba suspension for injection in pre-filled syringe

Meningococcal group B vaccine (recombinant, adsorbed)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

1 dose (0.5 ml) contains:

Neisseria meningitidis serogroup B fHbp subfamily A[1,2,3]	60 micrograms
Neisseria meningitidis serogroup B fHbp subfamily B[1,2,3]	60 micrograms

[1] Recombinant lipidated fHbp (factor H binding protein)
[2] Produced in *Escherichia coli* cells by recombinant DNA technology
[3] Adsorbed on aluminium phosphate (0.25 milligram aluminium per dose)

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Suspension for injection.
White liquid suspension.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Trumenba is indicated for active immunisation of individuals 10 years and older to prevent invasive meningococcal disease caused by *Neisseria meningitidis* serogroup B.

See section 5.1 for information on the immune response against specific serogroup B strains.

The use of this vaccine should be in accordance with official recommendations.

4.2 Posology and method of administration

Posology

Primary series
2 doses (0.5 ml each) administered at a 6 month interval (see section 5.1).

3 doses: 2 doses (0.5 ml each) administered at least 1 month apart, followed by a third dose at least 4 months after the second dose (see section 5.1).

Booster dose

A booster dose should be considered following either dosing regimen for individuals at continued risk of invasive meningococcal disease (see section 5.1).

Other paediatric population
Safety and efficacy of Trumenba in children below 10 years of age have not been established. No data are available.

Method of administration

For intramuscular injection only. The preferred site for injection is the deltoid muscle of the upper arm.

For instructions on the handling of the vaccine before administration, see section 6.6.

There are no data available on the interchangeability of Trumenba with other meningococcal group B vaccines to complete the vaccination series.

4.3 Contraindications

Hypersensitivity to the active substances or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

In order to improve the traceability of biological medicinal products, the tradename and batch number of the administered product should be clearly recorded (or stated) in the patient file.

Appropriate medical treatment and supervision should always be readily available in case of an anaphylactic event following the administration of the vaccine.

As with other injectable vaccines, syncope (fainting) can occur in association with administration of Trumenba. Procedures should be in place to avoid injury from fainting.

Vaccination should be postponed in individuals suffering from an acute severe febrile illness. However, the presence of a minor infection, such as cold, should not result in the deferral of vaccination.

Do not inject intravenously, intradermally, or subcutaneously.

Trumenba should not be given to individuals with thrombocytopenia or any coagulation disorder that would contraindicate intramuscular injection, unless the potential benefit clearly outweighs the risk of administration.

Persons with familial complement deficiencies (for example, C5 or C3 deficiencies) and persons receiving treatments that inhibit terminal complement activation (for example, eculizumab) are at increased risk for invasive disease caused by *Neisseria meningitidis* serogroup B, even if they develop antibodies following vaccination with Trumenba.

As with any vaccine, vaccination with Trumenba may not protect all vaccine recipients.

Limitations of clinical trials

There are no data on the use of Trumenba in immunocompromised individuals. Immunocompromised individuals, including individuals receiving immunosuppressant therapy, may have a diminished immune response to Trumenba.

There are no data on the use of Trumenba in subjects above 65 years of age.

4.5 Interaction with other medicinal products and other forms of interaction

Trumenba can be given concomitantly with any of the following vaccines: Tetanus Toxoid, Reduced Diphtheria Toxoid, Acellular Pertussis, and Inactivated Poliovirus Vaccine (TdaP-IPV), Quadrivalent Human Papillomavirus vaccine (HPV4), Meningococcal Serogroups A, C, Y, W conjugate vaccine (MenACWY) and Tetanus Toxoid, Reduced Diphtheria Toxoid, and Acellular Pertussis Vaccine Adsorbed (Tdap).

When given concomitantly with other vaccines Trumenba must be administered at a separate injection site.

Trumenba should not be mixed with other vaccines in the same syringe.

4.6 Fertility, pregnancy and lactation

Pregnancy

There are no data from the use of Trumenba in pregnant women. The potential risk for pregnant women is unknown. Nevertheless, vaccination should not be withheld when there is a clear risk of exposure to meningococcal infection.

Reproduction studies performed in female rabbits have revealed no evidence of impaired female fertility or harm to the foetus due to Trumenba.

Breast-feeding

It is unknown whether Trumenba is excreted in human milk. Trumenba should only be used during breast-feeding when the possible advantages outweigh the potential risks.

Fertility

Animal studies do not indicate direct or indirect harmful effects with respect to fertility in females (see section 5.3).

Trumenba has not been evaluated for impairment of fertility in males.

4.7 Effects on ability to drive and use machines

Trumenba has no or negligible influence on the ability to drive and use machines. However, some of the effects mentioned under section 4.8 may temporarily affect the ability to drive or use machines.

4.8 Undesirable effects

Summary of the safety profile

The safety profile presented is based on analysis of over 15,000 subjects (aged 10 years and older) who have been vaccinated with at least 1 dose of Trumenba in 11 completed clinical studies. The most common adverse reactions observed were injection site pain, redness and swelling at the vaccination site, headache, fatigue, chills, diarrhoea, muscle pain, joint pain, and nausea.

Adverse reactions following booster vaccination in 268 subjects aged 15 to 23 years were similar to adverse reactions during the primary Trumenba vaccination series approximately 4 years earlier.

List of adverse reactions

Adverse reactions reported in clinical studies are listed in decreasing order of frequency and seriousness according to the following frequency categories:

Very common (≥1/10)
Common (≥1/100 to <1/10)
Uncommon (≥1/1,000 to <1/100)
Rare (≥1/10,000 to <1/1,000)
Very rare (<1/10,000)
Not known (cannot be estimated from available data)

Immune system disorder
Not known: Allergic reactions*

Nervous system disorders
Very common: Headache

Gastrointestinal disorders
Very common: Diarrhoea; nausea
Common: Vomiting

Musculoskeletal and connective tissue disorders
Very common: Muscle pain (myalgia); joint pain (arthralgia)

General disorders and administration site conditions
Very common: Chills; fatigue; redness (erythema), swelling (induration) and pain at injection site
Common: Fever ≥38°C (Pyrexia)

* The following is considered an adverse reaction for Trumenba and was reported in the post-marketing experience. Because this reaction was derived from spontaneous reports, the frequency could not be determined and is thus considered as not known.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions.

4.9 Overdose

Experience of overdose is limited. In the event of overdose, monitoring of vital functions and possible symptomatic treatment is recommended.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: vaccines; ATC code: J07AH09

Mechanism of action

Trumenba is a vaccine composed of 2 recombinant lipidated factor H binding protein (fHbp) variants. fHbp is found on the surface of meningococcal bacteria and is essential for bacteria to avoid host immune defenses. fHbp variants segregate into 2 immunologically distinct subfamilies, A and B, and over 96% of meningococcal serogroup B isolates in Europe express fHbp variants from either subfamily on the bacterial surface.

Immunisation with Trumenba, which contains one fHbp variant each from subfamily A and B, is intended to stimulate the production of bactericidal antibodies that recognize fHbp expressed by meningococci. The Meningococcal Antigen Surface Expression (MEASURE) assay was developed to relate the level of fHbp surface expression to killing of meningococcal serogroup B strains in serum bactericidal assays with human complement (hSBAs). A survey of over 2,150 different invasive meningococcal serogroup B isolates collected from 2000-2014 in 7 European countries, the US and Canada demonstrated that over 91% of all meningococcal serogroup B isolates expressed sufficient levels of fHbp to be susceptible to bactericidal killing by vaccine-induced antibodies.

Clinical efficacy

The efficacy of Trumenba has not been evaluated through clinical trials. Vaccine efficacy has been inferred by demonstrating the induction of serum bactericidal antibody responses to 4 meningococcal serogroup B test strains (see the Immunogenicity section). The 4 test strains express fHbp variants representing the 2 subfamilies (A and B) and, when taken together, are representative of meningococcal serogroup B strains causing invasive disease.

Immunogenicity

Protection against invasive meningococcal disease is mediated by serum bactericidal antibodies to bacterial surface antigens. Bactericidal antibodies act in concert with human complement to kill meningococci. This process is measured *in vitro* with serum bactericidal assay using human complement (hSBA) for meningococcal serogroup B. An hSBA titre of greater than or equal 1:4 is assumed to be protective against meningococcal disease. In the immunogenicity analysis for Trumenba, a response was defined as an hSBA titre of at least 1:8 or 1:16 depending on the hSBA strain. A 4-fold increase in hSBA titre for each of the 4 primary meningococcal serogroup B test strains was defined as follows: (1) For subjects with a baseline hSBA titre <1:4, a 4-fold response was defined as an hSBA titre ≥1:16. (2) For subjects with a baseline hSBA titre ≥1:4, a 4-fold response was defined as an hSBA titre ≥4 times the lower limit of quantitation or ≥4 times the baseline titre, whichever was higher. A composite response was defined as a response for all 4 hSBA strains combined.

The immunogenicity of Trumenba following 2 or 3 vaccinations was evaluated in individuals 11 to 18 years of age in Europe (Study B1971012) and following 3 vaccinations in individuals 10 to 25 years of age globally (Studies B1971009 and B1971016).

In Study B1971012, Trumenba was administered according to the following schedules: Group 1 (0, 1, and 6 months); Group 2 (0, 2, and 6 months); Group 3 (0 and 6 months); Group 4 (0 and 2 months); Group 5 (0 and 4 months). Of the 1,713 subjects randomised, 427 were in Group 1, 430 were in Group 2, 427 were in Group 3, 286 were in Group 4, and 143 were in Group 5. All subjects received 4 study injections, either 2 or 3 doses of Trumenba and 1 or 2 doses of saline. The hSBA responses observed after the second or third dose for Groups 1, 2, and 3 are presented in Tables 1 and 2.

For the second and third doses, serum was obtained approximately 1 month after the second or third vaccination dose.

Table 1. Immune Responses Among Individuals 11 to 18 Years of Age Administered Trumenba After Various 2- and 3-Dose Schedules (Study B1971012)

		Group 1 (0, 1, and 6 Months)		Group 2 (0, 2, and 6 Months)		Group 3 (0 and 6 Months)	
		N	% (95% CI)	N	% (95% CI)	N	% (95% CI)
hSBA Strain (fHbp Variant)	**Dose**						
PMB80 (A22)	**% hSBA ≥1:16**						
	Dose 2	351	73.5 (68.6, 78.0)	344	88.1 (84.2, 91.3)	369	93.2 (90.2, 95.6)
	Dose 3	360	91.4 (88.0, 94.1)	357	95.0 (92.1, 97.0)	--	--
	≥4-Fold rise in hSBA titre (%)						
	Dose 2	343	55.7 (50.3, 61.0)	336	73.8 (68.8, 78.4)	362	80.7 (76.2, 84.6)
	Dose 3	351	78.1 (73.4, 82.3)	349	84.0 (79.7, 87.6)	--	--
PMB2001 (A56)	**% hSBA ≥1:8**						
	Dose 2	353	96.6 (94.1, 98.2)	339	97.9 (95.8, 99.2)	370	98.4 (96.5, 99.4)
	Dose 3	362	99.4 (98.0, 99.9)	359	98.9 (97.2, 99.7)	--	--
	≥4-Fold rise in hSBA titre (%)						
	Dose 2	338	86.1 (81.9, 89.6)	327	90.5 (86.8, 93.5)	354	90.4 (86.8, 93.3)
	Dose 3	347	93.4 (90.2, 95.8)	347	94.2 (91.2, 96.4)	--	--
PMB2948 (B24)	**% hSBA ≥1:8**						
	Dose 2	344	62.2 (56.9, 67.4)	337	70.3 (65.1, 75.2)	359	81.1 (76.6, 85.0)
	Dose 3	354	89.0 (85.2, 92.0)	354	88.4 (84.6, 91.6)	--	--
	≥4-Fold rise in hSBA titre (%)						
	Dose 2	341	47.2 (41.8, 52.7)	333	54.1 (48.5, 59.5)	357	65.5 (60.4, 70.5)
	Dose 3	351	74.6 (69.8, 79.1)	350	75.4 (70.6, 79.8)	--	--
PMB2707 (B44)	**% hSBA ≥1:8**						
	Dose 2	341	54.0 (48.5, 59.3)	331	61.9 (56.5, 67.2)	356	77.5 (72.8, 81.8)
	Dose 3	356	88.5 (84.7, 91.6)	352	86.1 (82.0, 89.5)	--	--
	≥4-Fold rise in hSBA titre (%)						
	Dose 2	339	43.4 (38.0, 48.8)	328	55.2 (49.6, 60.6)	355	66.8 (61.6, 71.6)
	Dose 3	354	82.2 (77.8, 86.0)	349	81.7 (77.2, 85.6)	--	--
Composite response (A response for all 4 hSBA strains combined)							

		Group 1 (0, 1, and 6 Months)		Group 2 (0, 2, and 6 Months)		Group 3 (0 and 6 Months)	
		N	% (95% CI)	N	% (95% CI)	N	% (95% CI)
hSBA Strain (fHbp Variant)	**Dose**						
	Before Dose 1	339	3.5 (1.8, 6.1)	333	2.4 (1.0, 4.7)	345	3.2 (1.6, 5.6)
	Dose 2	308	45.1 (39.5, 50.9)	311	54.3 (48.6, 60.0)	343	73.5 (68.5, 78.1)
	Dose 3	337	83.1 (78.6, 86.9)	345	81.7 (77.3, 85.7)	--	--
Abbreviations: hSBA=serum bactericidal assay using human complement; fHbp=factor H binding protein. Note: The lower limit of quantitation is an hSBA titre = 1:16 for PMB80 (A22) and 1:8 for PMB2001 (A56), PMB2948 (B24), and PMB2707 (B44).							

Table 2. Immune Responses Among Individuals 11 to 18 Years of Age Administered Trumenba After Various 2- and 3-Dose Schedules (Study B1971012)

		Group 1 (0, 1, and 6 Months)		Group 2 (0, 2, and 6 Months)		Group 3 (0 and 6 Months)	
		N	GMT (95% CI)	N	GMT (95% CI)	N	GMT (95% CI)
hSBA Strain (fHbp Variant)	**Dose**						
PMB80 (A22)	**hSBA GMT**						
	Dose 2	351	29.0 (26.0, 32.5)	344	35.6 (32.2, 39.4)	369	50.6 (45.9, 55.8)
	Dose 3	360	58.4 (52.4, 64.9)	357	58.3 (53.2, 63.9)	--	--
PMB2001 (A56)	**hSBA GMT**						
	Dose 2	353	77.3 (68.5, 87.1)	339	94.6 (84.6, 105.7)	370	125.6 (112.6, 140.2)
	Dose 3	362	152.9 (137.2, 170.5)	359	155.6 (140.4, 172.4)	--	--
PMB2948 (B24)	**hSBA GMT**						
	Dose 2	344	13.8 (12.2, 15.6)	337	14.9 (13.2, 16.7)	359	20.6 (18.4, 23.2)
	Dose 3	354	29.1 (25.9, 32.7)	354	25.6 (23.0, 28.5)	--	--
PMB2707 (B44)	**hSBA GMT**						
	Dose 2	341	13.1 (11.3, 15.1)	331	15.5 (13.5, 17.9)	356	22.5 (19.6, 25.7)
	Dose 3	356	40.3 (35.2, 46.1)	352	35.0 (30.6, 39.9)	--	--
Abbreviations: GMT=geometric mean titre; hSBA=serum bactericidal assay using human complement; fHbp=factor H binding protein.							

Study B1971009 was a Phase 3, randomised, active-controlled, observer-blinded, multicentre trial in which subjects aged 10 to 18 years received 1 of 3 lots (Groups 1, 2, and 3) of Trumenba or the active control hepatitis A virus (HAV) vaccine/saline. A total of 2,693 subjects received at least 1 dose of Trumenba and 897 received at least 1 dose of HAV

vaccine/saline. The study assessed the safety, tolerability, immunogenicity, and demonstration of manufacturability of 3 lots of Trumenba administered on a 0-, 2-, and 6-month schedule. The hSBA responses observed after the third dose in Group 1 are presented in Tables 3 and 4. Results from Groups 2 and 3 are not presented, as only 2 representative strains were evaluated. Similar results were observed in Groups 2 and 3 as observed in Group 1.

Study B1971016 was a Phase 3, randomised, placebo-controlled, observer-blinded, multicentre trial in which subjects 18 to 25 years of age were assigned to 2 groups in a 3:1 ratio (Group 1:Group 2). Group 1 received Trumenba at months 0, 2, and 6. Group 2 received saline at months 0, 2, and 6. A total of 2,471 subjects received Trumenba and 822 received saline. The hSBA responses observed after the third dose in Groups 1 and 2 are presented in Tables 3 and 4.

Serum was obtained approximately 1 month after vaccination.

Table 3. Immune Responses Among Individuals 10 to 25 Years of Age 1 Month Following the Third Dose of Trumenba or Control Given on a 0-, 2-, 6-Month Schedule (Study B1971009 and Study B1971016)

		Study B1971009 (10-18 years of age)				**Study B1971016 (18-25 years of age)**			
		Group 1		**Group 4**		**Group 1**		**Group 2**	
		Trumenba		**HAV/saline**		**Trumenba**		**Saline**	
hSBA Strain (fHbp Variant)		**N**	**% (95% CI)**	**N**	**% (95% CI)**	**N**	**% (95% CI)**	**N**	**% (95% CI)**
PMB80 (A22)	**% hSBA ≥1:16**								
		1266	97.8 (96.8, 98.5)	749	34.0 (30.7, 37.6)	1714	93.5 (92.2, 94.6)	577	36.6 (32.6, 40.6)
	≥4-Fold rise in hSBA titre (%)								
		1225	83.2 (81.0, 85.2)	730	9.6 (7.6, 12.0)	1695	80.5 (78.6, 82.4)	568	6.3 (4.5, 8.7)
PMB2001 (A56)	**% hSBA ≥1:8**								
		1229	99.5 (98.9, 99.8)	363	27.5 (23.0, 32.5)	1708	99.4 (98.9, 99.7)	552	34.2 (30.3, 38.4)
	≥4-Fold rise in hSBA titre (%)								
		1128	90.2 (88.4, 91.9)	337	11.3 (8.1, 15.1)	1642	90.0 (88.4, 91.4)	533	10.3 (7.9, 13.2)
PMB2948 (B24)	**% hSBA ≥1:8**								
		1250	87.1 (85.1, 88.9)	762	7.0 (5.3, 9.0)	1702	95.1 (93.9, 96.0)	573	30.2 (26.5, 34.1)
	≥4-Fold rise in hSBA titre (%)								
		1235	79.8 (77.4, 82.0)	752	2.7 (1.6, 4.1)	1675	79.3 (77.3, 81.2)	562	5.5 (3.8, 7.7)
PMB2707 (B44)	**% hSBA ≥1:8**								
		1210	89.3 (87.4, 90.9)	393	5.3 (3.3, 8.1)	1703	87.4 (85.8, 89.0)	577	11.4 (9.0, 14.3)
	≥4-Fold rise in hSBA titre (%)								
		1203	85.9 (83.8, 87.8)	391	1.0 (0.3, 2.6)	1696	79.6 (77.6, 81.5)	573	1.6 (0.7, 3.0)
Composite response (A response for all 4 hSBA strains combined)									
	Before Dose 1	1088	1.1 (0.6, 1.9)	354	2.0 (0.8, 4.0)	1612	7.3 (6.0, 8.6)	541	6.1 (4.2, 8.5)
	Dose 3	1170	83.5 (81.3, 85.6)	353	2.8 (1.4, 5.1)	1664	84.9 (83.1, 86.6)	535	7.5 (5.4, 10.0)

Abbreviations: hSBA=serum bactericidal assay using human complement; fHbp=factor H binding protein.
Note: The lower limit of quantitation is an hSBA titre = 1:16 for PMB80 (A22) and 1:8 for PMB2001 (A56), PMB2948 (B24), and PMB2707 (B44).

Table 4. Immune Responses Among Individuals 10 to 25 Years of Age 1 Month Following the Third Dose of Trumenba or Control Given on a 0-, 2-, 6-Month Schedule (Study B1971009 and B1971016)

	Study B1971009 (10-18 years of age)				**Study B1971016 (18-25 years of age)**			
	Group 1		**Group 4**		**Group 1**		**Group 2**	
	Trumenba		**HAV/saline**		**Trumenba**		**Saline**	
hSBA Strain (fHbp Variant)	**N**	**GMT (95% CI)**	**N**	**GMT (95% CI)**	**N**	**GMT (95% CI)**	**N**	**GMT (95% CI)**
PMB80 (A22)	1266	86.8 (82.3, 91.5)	749	12.6 (12.0, 13.4)	1714	74.3 (70.2, 78.6)	577	13.2 (12.4, 14.1)
PMB2001 (A56)	1229	222.5 (210.1, 235.6)	363	8.8 (7.6, 10.1)	1708	176.7 (167.8, 186.1)	552	9.1 (8.2, 10.1)
PMB2948 (B24)	1250	24.1 (22.7, 25.5)	762	4.5 (4.4, 4.7)	1702	49.5 (46.8, 52.4)	573	7.2 (6.6, 7.8)
PMB2707 (B44)	1210	50.9 (47.0, 55.2)	393	4.4 (4.2, 4.6)	1703	47.6 (44.2, 51.3)	577	4.8 (4.6, 5.1)
Abbreviations: GMT=geometric mean titre; hSBA=serum bactericidal assay using human complement; fHbp=factor H binding protein.								

In Studies B1971009 and B1971016, the proportion of subjects achieving a defined hSBA titre after 3 doses of Trumenba, administered on a 0-, 2-, and 6-month schedule, was evaluated against a panel of 10 additional strains, each expressing a different fHbp variant (Table 5). These additional hSBAs support and extend the breadth of vaccine coverage demonstrated by the 4 representative primary strains (Tables 3 and 4).

Serum was obtained approximately 1 month after vaccination.

Table 5. Immune Responses Among Individuals 10 to 25 Years of Age Against 10 Additional Strains 1 Month Following the Third Dose of Trumenba Given on a 0-, 2-, 6-Month Schedule (Study B1971009 and Study B1971016)

	Study B1971009 (10 to 18 Years of Age)		**Study B1971016 (18 to 25 Years of Age)**	
	N	**% (95% CI)**	**N**	**% (95% CI)**
hSBA Strain (fHbp Variant)				
	% hSBA ≥1:8			
PMB3040 (A07)	280	96.4 (93.5, 98.3)	277	95.7 (92.6, 97.7)
PMB1672 (A15)	266	87.2 (82.6, 91.0)	279	91.8 (87.9, 94.7)
PMB3175 (A29)	278	98.6 (96.4, 99.6)	283	99.3 (97.5, 99.9)
PMB1256 (B03)	279	92.5 (88.7, 95.3)	273	86.4 (81.8, 90.3)
PMB866 (B09)	276	86.2 (81.6, 90.1)	274	77.0 (71.6, 81.9)
PMB431 (B15)	281	98.2 (95.9, 99.4)	276	96.7 (93.9, 98.5)
PMB648 (B16)	278	81.7 (76.6, 86.0)	273	78.0 (72.6, 82.8)

	Study B1971009 (10 to 18 Years of Age)		Study B1971016 (18 to 25 Years of Age)	
	N	% (95% CI)	N	% (95% CI)
hSBA Strain (fHbp Variant)				
	% hSBA ≥1:16			
PMB3010 (A06)	280	95.7 (92.6, 97.8)	275	92.0 (88.1, 94.9)
PMB824 (A12)	277	75.1 (69.6, 80.1)	275	71.3 (65.5, 76.5)
PMB1989 (A19)	275	92.7 (89.0, 95.5)	284	95.8 (92.7, 97.8)
Abbreviations: hSBA=serum bactericidal assay using human complement; fHbp=factor H binding protein.				

Persistence of immunity and response to booster vaccination

Study B1971033 is an open-label, follow-up study of subjects previously enrolled in a primary study, including Study B1971012. Subjects attended visits over 4 years for collection of blood samples and received a single booster dose of Trumenba approximately 4 years after receipt of a primary series of 2 or 3 doses of Trumenba. The hSBA responses for subjects enrolled from primary Study B1971012 Group 1 (0-, 1-, 6-Month Schedule), Group 2 (0-, 2-, 6-Month) and Group 3 (0-, 6-Month) are presented in Tables 6 and 7. A booster response in hSBA responses at 1 month following a dose of Trumenba approximately 4 years after a primary series of 2 doses (Group 3) or 3 doses (Groups 1 and 2) was observed.

Table 6. Persistence of Immune and Booster Responses Among Individuals 11 to 18 Years of Age Administered a Primary Series of Trumenba on a 0-, 1-, 6-Month-; 0-, 2-, 6-Month- and 0-, 6-Month Schedule and a Booster 4 Years After Primary Series (Study B1971033)

		Primary Study B1971012 Vaccine Group (as Randomised)					
		Group 1 (0, 1, and 6 Months)		Group 2 (0, 2, and 6 Months)		Group 3 (0 and 6 Months)	
		N	% (95% CI)	N	% (95% CI)	N	% (95% CI)
hSBA Strain (fHbp Variant)	**Time Point**						
PMB80 (A22)	**% hSBA ≥1:16**						
	1 Month after last primary Dose	100	91.0 (83.6, 95.8)	113	92.0 (85.4, 96.3)	115	96.5 (91.3, 99.0)
	12 Months after last primary Dose	99	41.4 (31.6, 51.8)	111	45.0 (35.6, 54.8)	113	36.3 (27.4, 45.9)
	48 Months after last primary Dose	90	41.1 (30.8, 52.0)	100	43.0 (33.1, 53.3)	101	39.6 (30.0, 49.8)
	1 Month after booster Dose	59	98.3 (90.9, 100.0)	58	100.0 (93.8, 100.0)	62	95.2 (86.5, 99.0)
PMB2001 (A56)	**% hSBA ≥1:8**						
	1 Month after last primary Dose	100	100.0 (96.4, 100.0)	112	99.1 (95.1, 100.0)	116	99.1 (95.3, 100.0)
	12 Months after last primary Dose	98	73.5 (63.6, 81.9)	109	76.1 (67.0, 83.8)	106	60.4 (50.4, 69.7)

		Primary Study B1971012 Vaccine Group (as Randomised)					
		Group 1		Group 2		Group 3	
		(0, 1, and 6 Months)		(0, 2, and 6 Months)		(0 and 6 Months)	
		N	% (95% CI)	N	% (95% CI)	N	% (95% CI)
hSBA Strain (fHbp Variant)	**Time Point**						
	48 Months after last primary Dose	85	47.1 (36.1, 58.2)	99	58.6 (48.2, 68.4)	99	57.6 (47.2, 67.5)
	1 Month after booster Dose	59	100.0 (93.9, 100.0)	58	100.0 (93.8, 100.0)	62	98.4 (91.3, 100.0)
PMB2948 (B24)	**% hSBA ≥1:8**						
	1 Month after last primary Dose	100	90.0 (82.4, 95.1)	114	88.6 (81.3, 93.8)	113	81.4 (73.0, 88.1)
	12 Months after last primary Dose	98	40.8 (31.0, 51.2)	108	49.1 (39.3, 58.9)	103	36.9 (27.6, 47.0)
	48 Months after last primary Dose	90	41.1 (30.8, 52.0)	98	40.8 (31.0, 51.2)	105	30.5 (21.9, 40.2)
	1 Month after booster Dose	59	100.0 (93.9, 100.0)	58	100.0 (93.8, 100.0)	61	93.4 (84.1, 98.2)
PMB2707 (B44)	**% hSBA ≥1:8**						
	1 Month after last primary Dose	99	88.9 (81.0, 94.3)	111	87.4 (79.7, 92.9)	113	77.9 (69.1, 85.1)
	12 Months after last primary Dose	100	24.0 (16.0, 33.6)	111	22.5 (15.1, 31.4)	115	16.5 (10.3, 24.6)
	48 Months after last primary Dose	92	20.7 (12.9, 30.4)	100	18.0 (11.0, 26.9)	106	18.9 (11.9, 27.6)
	1 Month after booster Dose	59	94.9 (85.9, 98.9)	57	98.2 (90.6, 100.0)	62	91.9 (82.2, 97.3)
Composite response (A response for all 4 hSBA strains combined)							
	1 Month after last primary Dose	57	80.7 (68.1, 90.0)	55	87.3 (75.5, 94.7)	57	77.2 (64.2, 87.3)
	12 Months after last primary Dose	55	10.9 (4.1, 22.2)	51	13.7 (5.7, 26.3)	49	20.4 (10.2, 34.3)
	48 Months after last primary Dose	51	15.7 (7.0, 28.6)	55	18.2 (9.1, 30.9)	55	16.4 (7.8, 28.8)
	1 Month after booster Dose	59	93.2 (83.5, 98.1)	57	98.2 (90.6, 100.0)	61	91.8 (81.9, 97.3)

Abbreviations: hSBA=serum bactericidal assay using human complement; fHbp=factor H binding protein.
Note: The lower limit of quantitation is an hSBA titre = 1:16 for PMB80 (A22) and 1:8 for PMB2001 (A56), PMB2948 (B24), and PMB2707 (B44).

Table 7. Persistence of Immune and Booster Responses Among Individuals 11 to 18 Years of Age Administered a Primary Series of Trumenba on a 0-, 1-, 6-Month-; 0-, 2-, 6-Month- and 0-, 6-Month Schedule and a Booster 4 Years After Primary Series (Study B1971033)

	Primary Study B1971012 Vaccine Group (as Randomised)		
	Group 1	Group 2	Group 3
	(0, 1, and 6 Months)	(0, 2, and 6 Months)	(0 and 6 Months)

		N	GMT (95% CI)	N	GMT (95% CI)	N	GMT (95% CI)
hSBA Strain (fHbp Variant)	**Time Point**						
PMB80 (A22)	**hSBA GMT**						
	1 Month after last primary Dose	100	60.1 (48.6, 74.4)	113	56.6 (47.0, 68.2)	115	54.7 (47.3, 63.3)
	12 Months after last primary Dose	99	14.9 (12.6, 17.7)	111	15.8 (13.4, 18.6)	113	15.6 (13.0, 18.8)
	48 Months after last primary Dose	90	14.3 (11.9, 17.0)	100	15.1 (12.7, 18.0)	101	14.8 (12.5, 17.6)
	1 Month after booster Dose	59	90.0 (69.6, 116.3)	58	119.1 (90.0, 157.8)	62	140.0 (104.2, 187.9)
PMB2001 (A56)	**hSBA GMT**						
	1 Month after last primary Dose	100	199.5 (162.7, 244.5)	112	196.2 (161.8, 237.9)	116	142.5 (118.3, 171.7)
	12 Months after last primary Dose	98	25.7 (19.4, 34.0)	109	27.3 (21.0, 35.4)	106	18.5 (13.8, 24.7)
	48 Months after last primary Dose	85	11.5 (8.6, 15.5)	99	17.5 (13.2, 23.3)	99	16.0 (12.1, 21.1)
	1 Month after booster Dose	59	335.4 (262.1, 429.2)	58	370.8 (275.8, 498.6)	62	358.0 (262.1, 489.0)
PMB2948 (B24)	**hSBA GMT**						
	1 Month after last primary Dose	100	29.7 (23.9, 36.8)	114	30.9 (25.3, 37.7)	113	28.0 (22.0, 35.5)
	12 Months after last primary Dose	98	9.7 (7.5, 12.4)	108	11.5 (9.0, 14.6)	103	8.4 (6.7, 10.6)
	48 Months after last primary Dose	90	9.4 (7.3, 12.1)	98	9.7 (7.6, 12.3)	105	7.5 (6.1, 9.2)
	1 Month after booster Dose	59	74.6 (55.9, 99.5)	58	80.3 (62.6, 103.1)	61	86.0 (62.6, 118.2)
PMB2707 (B44)	**hSBA GMT**						
	1 Month after last primary Dose	99	50.1 (38.0, 66.1)	111	41.9 (32.3, 54.3)	113	31.4 (23.9, 41.3)
	12 Months after last primary Dose	100	6.4 (5.2, 7.8)	111	6.0 (5.1, 7.2)	115	5.6 (4.8, 6.5)
	48 Months after last primary Dose	92	6.0 (5.0, 7.2)	100	5.3 (4.6, 6.1)	106	5.1 (4.6, 5.7)
	1 Month after booster Dose	59	109.9 (74.5, 162.0)	57	117.6 (84.5, 163.5)	62	84.6 (57.8, 124.0)
Abbreviations: GMT=geometric mean titre; hSBA=serum bactericidal assay using human complement; fHbp=factor H binding protein.							

5.2 Pharmacokinetic properties

Not applicable.

5.3 Preclinical safety data

Non-clinical data revealed no special hazard for humans based on conventional studies of repeated dose toxicity and reproduction and developmental toxicity.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium Chloride
Histidine
Polysorbate 80 (E433)
Water for injections
For adsorbent, see section 2.

6.2 Incompatibilities

Do not mix Trumenba with other vaccines or medicinal products in the same syringe.

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

6.3 Shelf life

Please refer to the carton for recommended shelf-life.

6.4 Special precautions for storage

Store in a refrigerator (2°C-8°C).
Syringes should be stored in the refrigerator horizontally to minimize the re-dispersion time.
Do not freeze.

6.5 Nature and contents of container

0.5 ml suspension in a pre-filled syringe (Type I glass) with plastic Luer Lok adapter, chlorobutyl rubber plunger stopper, and a synthetic isoprene bromobutyl rubber tip cap with a plastic rigid tip cap cover with needle. The tip cap and rubber plunger of the pre-filled syringe are not made with natural rubber latex.

Pack size of 1 pre-filled syringe, with needle.

6.6 Special precautions for disposal and other handling

During storage, a white deposit and clear supernatant may be observed in the pre-filled syringe containing the suspension.

Before use, the pre-filled syringe should be shaken vigorously to ensure that a homogeneous white suspension is obtained.

Do not use the vaccine if it cannot be re-suspended.

The vaccine should be visually inspected for particulate matter and discoloration prior to administration. In the event of any foreign particulate matter and/or variation of physical aspect being observed, do not administer the vaccine.

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

January 2019
Hong Kong