FACT SHEET FOR HEALTHCARE PROVIDERS ADMINISTERING VACCINE (VACCINATION PROVIDERS)

EMERGENCY USE AUTHORIZATION (EUA) OF THE NOVAVAX COVID-19 VACCINE, ADJUVANTED TO PREVENT CORONAVIRUS DISEASE 2019 (COVID-19)

The U.S. Food and Drug Administration (FDA) has issued an Emergency Use Authorization (EUA) to permit the emergency use of the unapproved product, Novavax COVID-19 Vaccine, Adjuvanted, for active immunization to prevent COVID-19 in individuals 12 years of age and older.

SUMMARY OF INSTRUCTIONS FOR COVID-19 VACCINATION PROVIDERS

Vaccination providers enrolled in the federal COVID-19 Vaccination Program must report all vaccine administration errors, all serious adverse events, cases of myocarditis, cases of pericarditis, cases of Multisystem Inflammatory Syndrome (MIS) in adults and children, and cases of COVID-19 that result in hospitalization or death following administration of the Novavax COVID-19 Vaccine, Adjuvanted. See "MANDATORY REQUIREMENTS FOR THE NOVAVAX COVID-19 VACCINE, ADJUVANTED ADMINISTRATION UNDER EMERGENCY USE AUTHORIZATION" for reporting requirements.

The Novavax COVID-19 Vaccine, Adjuvanted is a suspension for intramuscular injection.

Primary Series

The Novavax COVID-19 Vaccine, Adjuvanted is authorized for emergency use to provide a two-dose primary series to individuals 12 years of age and older. The primary series of the Novavax COVID-19 Vaccine, Adjuvanted is two doses (0.5 mL each) given 3 weeks apart.

Booster Dose

The Novavax COVID-19 Vaccine, Adjuvanted is authorized for emergency use to provide a first booster dose to individuals 18 years of age and older for whom an FDA-authorized mRNA bivalent[1] COVID-19 booster vaccine is not accessible or clinically appropriate, and to individuals 18 years of age and older who elect to receive the Novavax COVID-19 Vaccine, Adjuvanted because they would otherwise not receive a booster dose of a COVID-19 vaccine.

For these individuals, a booster dose (0.5 mL) of Novavax COVID-19 Vaccine, Adjuvanted may be administered at least 6 months after completion of primary vaccination with an authorized or approved COVID-19 vaccine.

[1] Authorized bivalent COVID-19 vaccines encode the spike protein of the Original SARS-CoV-2 and the Omicron BA.4/BA.5 SARS-CoV-2

See this Fact Sheet for instructions for preparation and administration. This Fact Sheet may have been updated. For the most recent Fact Sheet, please see http://www.NovavaxCovidVaccine.com.

For information on clinical trials that are testing the use of the Novavax COVID-19 Vaccine, Adjuvanted for active immunization against COVID-19, please see http://www.clinicaltrials.gov.

DESCRIPTION OF COVID-19

Coronavirus disease 2019 (COVID-19) is an infectious disease caused by the novel coronavirus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), that appeared in late 2019. It is predominantly a respiratory illness that can affect other organs. People with COVID-19 have reported a wide range of symptoms, ranging from mild symptoms to severe illness. Symptoms may appear 2 to 14 days after exposure to the virus. Symptoms may include: fever or chills; cough; shortness of breath; fatigue; muscle or body aches; headache; new loss of taste or smell; sore throat; congestion or runny nose; nausea or vomiting; diarrhea.

DOSAGE AND ADMINISTRATION

Storage and Handling

Storage of Unpunctured Vial

Store the unpunctured multi-dose vial in a refrigerator between 2 to 8°C (36 to 46°F).

Do not freeze.

Protect from light.

Storage After First Puncture of the Vaccine Vial

After the first needle puncture, hold the vial between 2 to 25°C (36 to 77°F) for up to 6 hours. Discard the vial 6 hours after the first puncture.

Dosing and Schedule

Primary Series

The Novavax COVID-19 Vaccine, Adjuvanted is administered intramuscularly as a primary series of two doses (0.5 mL each) 3 weeks apart in individuals 12 years of age and older.

Booster Dose

A first booster dose (0.5 mL) of Novavax COVID-19 Vaccine, Adjuvanted may be administered intramuscularly at least 6 months after completion of primary vaccination with an authorized or approved COVID-19 vaccine in individuals 18 years of age and older for whom an FDA-authorized mRNA bivalent COVID-19 booster vaccine is not accessible or clinically appropriate and in individuals 18 years of age and older who elect to receive the Novavax COVID-19 Vaccine Adjuvanted because they would otherwise not receive a booster dose of a COVID-19 vaccine.

Dose Preparation

Inspect the vial

- The Novavax COVID-19 Vaccine, Adjuvanted is a colorless to slightly yellow, clear to mildly opalescent suspension, free from visible particles.
- Gently swirl the multi-dose vial before each dose withdrawal. Do not shake.
- Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. Do not administer the vaccine if either of these conditions exist.

Prepare for administration

- Record the date and time of the first puncture on the vial label.
- Novavax COVID-19 Vaccine, Adjuvanted is available in two presentations:
    - Multi-dose vial containing 5 doses of 0.5 mL each
    - Multi-dose vial containing 10 doses of 0.5 mL each
- Do not pool excess vaccine from multiple vials.
- After the first needle puncture, hold the vial between 2 to 25°C (36 to 77°F) for up to 6 hours.
- Discard vial 6 hours after the first puncture.

Administration

Administer the Novavax COVID-19 Vaccine, Adjuvanted intramuscularly.

CONTRAINDICATIONS

Do not administer the Novavax COVID-19 Vaccine, Adjuvanted to individuals with a known history of a severe allergic reaction (e.g., anaphylaxis) to any component of the Novavax COVID-19 Vaccine, Adjuvanted (*see Full EUA Prescribing Information*).

WARNINGS

Management of Acute Allergic Reactions

Appropriate medical treatment to manage immediate allergic reactions must be immediately available in the event an acute anaphylactic reaction occurs following administration of the Novavax COVID-19 Vaccine, Adjuvanted.

Monitor the Novavax COVID-19 Vaccine, Adjuvanted recipients for the occurrence of immediate adverse reactions according to the Centers for Disease Control (CDC) and Prevention guidelines (https://www.cdc.gov/vaccines/covid-19/clinical-considerations/managing-anaphylaxis.html).

Myocarditis and Pericarditis

Clinical trials data provide evidence for increased risks of myocarditis and pericarditis following administration of Novavax COVID-19 Vaccine, Adjuvanted (*see Full EUA Prescribing Information*).

The CDC has published considerations related to myocarditis and pericarditis after vaccination, including for vaccination of individuals with a history of myocarditis or pericarditis (https://www.cdc.gov/vaccines/covid-19/clinical-considerations/interim-considerations-us.html#myocarditis-pericarditis).

Syncope

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

Altered Immunocompetence

Immunocompromised persons, including individuals receiving immunosuppressant therapy, may have a diminished immune response to the Novavax COVID-19 Vaccine, Adjuvanted.

Limitations of Vaccine Effectiveness

The Novavax COVID-19 Vaccine, Adjuvanted may not protect all vaccine recipients.

ADVERSE REACTIONS

Adverse Reactions in Clinical Trials

Adverse reactions reported in clinical trials following administration of the Novavax COVID-19 Vaccine, Adjuvanted include injection site pain/tenderness, fatigue/malaise, muscle pain, headache, joint pain, nausea/vomiting, injection site redness, injection site swelling, fever, chills, injection site pruritus, hypersensitivity reactions, lymphadenopathy-related reactions, myocarditis, and pericarditis. (see *Full EUA Prescribing Information*).

Adverse Reactions Identified during Post-Authorization Use

Myocarditis, pericarditis, anaphylaxis, paresthesia, and hypoesthesia have been reported following administration of the Novavax COVID-19 Vaccine, Adjuvanted outside of clinical trials.

Additional adverse reactions, some of which may be serious, may become apparent with more widespread use of the Novavax COVID-19 Vaccine, Adjuvanted.

USE WITH OTHER VACCINES

There is no information on co-administration of the Novavax COVID-19 Vaccine, Adjuvanted with other vaccines.

INFORMATION TO PROVIDE TO VACCINE RECIPIENTS/CAREGIVERS

As the vaccination provider, you must communicate to the recipient or their caregiver, information consistent with the "Fact Sheet for Recipients and Caregivers" (and provide a copy or direct the individual to the website http://www.NovavaxCovidVaccine.com to obtain the Fact Sheet) prior to the individual receiving each dose of the Novavax COVID-19 Vaccine, Adjuvanted, including:

- FDA has authorized the emergency use of the Novavax COVID-19 Vaccine, Adjuvanted, which is not an FDA-approved vaccine.
- The recipient or their caregiver has the option to accept or refuse the Novavax COVID-19 Vaccine, Adjuvanted.
- The significant known and potential risks and benefits of the Novavax COVID-19 Vaccine, Adjuvanted, and the extent to which such risks and benefits are unknown.
- Information about available alternative vaccines and the risks and benefits of those alternatives.

For information on clinical trials that are evaluating the use of the Novavax COVID-19 Vaccine, Adjuvanted to prevent COVID-19, please see www.clinicaltrials.gov.

Provide a vaccination card to the recipient or their caregiver with the date when the recipient needs to return for the second dose of the Novavax COVID-19 Vaccine, Adjuvanted.

Provide the **V-safe** information sheet to vaccine recipients/caregivers and encourage vaccine recipients to participate in v-safe. **V-safe** is a voluntary smartphone-based tool that uses text messaging and web surveys to check in with people who have been vaccinated to identify potential side effects after COVID-19 vaccination. **V-safe** asks questions that help CDC monitor the safety of COVID-19 vaccines. **V-safe** also provides second-dose reminders if needed and live telephone follow-up by CDC if participants report a significant health impact following COVID-19 vaccination. For more information, visit: www.cdc.gov/vsafe.

MANDATORY REQUIREMENTS FOR THE NOVAVAX COVID-19 VACCINE, ADJUVANTED ADMINISTRATION UNDER EMERGENCY USE AUTHORIZATION

In order to mitigate the risks of using this unapproved product under EUA and to optimize the potential benefit of the Novavax COVID-19 Vaccine, Adjuvanted, the following items are required. Use of the unapproved Novavax COVID-19 Vaccine, Adjuvanted for active immunization to prevent COVID-19 under this EUA is limited to the following (all requirements **must** be met):

1. The Novavax COVID-19 Vaccine, Adjuvanted is authorized for use in individuals 12 years of age and older.

2. The vaccination provider must communicate to the individual receiving the Novavax COVID-19 Vaccine, Adjuvanted or their caregiver, information consistent with the "Fact Sheet for Recipients and Caregivers" prior to the individual receiving the Novavax COVID-19 Vaccine, Adjuvanted.

3. The vaccination provider must include vaccination information in the state/local jurisdiction's Immunization Information System (IIS) or other designated system.

4. The vaccination provider is responsible for mandatory reporting of the following to the Vaccine Adverse Event Reporting System (VAERS):

   - vaccine administration errors whether or not associated with an adverse event,
   - serious adverse events* (irrespective of attribution to vaccination),
   - cases of myocarditis,
   - cases of pericarditis,
   - cases of Multisystem Inflammatory Syndrome (MIS) in adults and children, and
   - cases of COVID-19 that result in hospitalization or death.

   Complete and submit reports to VAERS online at https://vaers.hhs.gov/reportevent.html. For further assistance with reporting to VAERS, call 1-800-822-7967. The reports should include the words "Novavax COVID-19 Vaccine, Adjuvanted EUA" in the description section of the report.

5. The vaccination provider is responsible for responding to FDA requests for information about vaccine administration errors, adverse events, cases of myocarditis, cases of pericarditis, cases of MIS in adults and children and cases of COVID-19 that result in hospitalization or death following administration of the Novavax COVID-19 Vaccine, Adjuvanted to recipients.

   *Serious adverse events are defined as:

   - Death;
   - A life-threatening adverse event;
   - Inpatient hospitalization or prolongation of existing hospitalization;
   - A persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions;
   - A congenital anomaly/birth defect;
   - An important medical event that based on appropriate medical judgment may jeopardize the individual and may require medical or surgical intervention to prevent one of the outcomes listed above.

OTHER ADVERSE EVENT REPORTING TO VAERS AND NOVAVAX, INC.

Vaccination providers may report to VAERS other adverse events that are not required to be reported using the contact information above.

To the extent feasible, report adverse events to Novavax, Inc. using the contact information below or by providing a copy of the VAERS form to Novavax, Inc.

Website	Fax number	Telephone number
www.NovavaxMedInfo.com	1-888-988-8809	1-844-NOVAVAX (1-844-668-2829)

ADDITIONAL INFORMATION

For general questions, visit the website or call the telephone number provided below.

To access the most recent Novavax COVID-19 Vaccine, Adjuvanted Fact Sheets, please scan the QR code or visit the website provided below.

Website	Telephone number
www.NovavaxCovidVaccine.com	1-844-NOVAVAX (1-844-668-2829)

AVAILABLE ALTERNATIVES

COMIRNATY (COVID-19 Vaccine, mRNA) and SPIKEVAX (COVID-19 Vaccine, mRNA) are FDA-approved vaccines to prevent COVID-19 caused by SARS-CoV-2. There may be clinical trials or availability under EUA of other COVID-19 vaccines.

FEDERAL COVID-19 VACCINATION PROGRAM

This vaccine is being made available for emergency use exclusively through the CDC COVID-19 Vaccination Program (the Vaccination Program). Healthcare providers must enroll as providers in the Vaccination Program and comply with the provider requirements. Vaccination providers may not charge any fee for the vaccine and may not charge the vaccine recipient any out-of-pocket charge for administration. However, vaccination providers may seek appropriate reimbursement from a program or plan that covers COVID-19 vaccine administration fees for the vaccine recipient (private insurance, Medicare, Medicaid, HRSA COVID-19 Uninsured Program for non-insured recipients). For information regarding provider requirements and enrollment in the CDC COVID-19 Vaccination Program, see https://www.cdc.gov/vaccines/covid-19/provider-enrollment.html.

Individuals becoming aware of any potential violations of the CDC COVID-19 Vaccination Program requirements are encouraged to report them to the Office of the Inspector General, U.S. Department of Health and Human Services, at 1-800-HHS-TIPS or TIPS.HHS.GOV.

AUTHORITY FOR ISSUANCE OF THE EUA

The Secretary of the Department of Health and Human Services (HHS) has declared a public health emergency that justifies the emergency use of drugs and biological products during the COVID-19 Pandemic. In response, the FDA has issued an EUA for the unapproved product, Novavax COVID-19 Vaccine, Adjuvanted, for active immunization to prevent COVID-19 in individuals 12 years of age and older.

FDA issued this EUA based on Novavax, Inc.'s request and submitted data.

Although limited scientific information is available, based on the totality of the scientific evidence available to date, it is reasonable to believe that the Novavax COVID-19 Vaccine, Adjuvanted may be effective for the prevention of COVID-19 in individuals as specified in the *Full EUA Prescribing Information*.

This EUA for the Novavax COVID-19 Vaccine, Adjuvanted will end when the Secretary of HHS determines that the circumstances justifying the EUA no longer exist or when there is a change in the approval status of the product such that an EUA is no longer needed.

For additional information about EUA, visit FDA at: https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization.

COUNTERMEASURES INJURY COMPENSATION PROGRAM

The Countermeasures Injury Compensation Program (CICP) is a federal program that has been created to help pay for related costs of medical care and other specific expenses to compensate people injured after use of certain medical countermeasures. Medical countermeasures are specific vaccines, medications, devices, or other items used to prevent, diagnose, or treat the public during a public health emergency or a security threat. For more information about CICP, visit http://www.hrsa.gov/cicp, email cicp@hrsa.gov, or call: 1-855-266-2427.

Manufactured for:
Novavax, Inc., Gaithersburg, MD, 20878

C20001US-00X

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END SHORT VERSION FACT SHEET

Long Version (Full EUA Prescribing Information) Begins On Next Page

FULL EMERGENCY USE AUTHORIZATION (EUA) PRESCRIBING INFORMATION

NOVAVAX COVID-19 VACCINE, ADJUVANTED

FULL EMERGENCY USE AUTHORIZATION (EUA) PRESCRIBING INFORMATION: CONTENTS*

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

FULL EMERGENCY USE AUTHORIZATION (EUA) PRESCRIBING INFORMATION

1 AUTHORIZED USE

The Novavax COVID-19 Vaccine, Adjuvanted is authorized for use under an Emergency Use Authorization (EUA) for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 12 years of age and older.

2 DOSAGE AND ADMINISTRATION

For intramuscular injection only.

2.1 Preparation for Administration

Inspect the vial

- The Novavax COVID-19 Vaccine, Adjuvanted is a colorless to slightly yellow, clear to mildly opalescent suspension, free from visible particles.
- Gently swirl the multi-dose vial before each dose withdrawal. Do not shake.
- Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. Do not administer the vaccine if either of these conditions exist.

Prepare for administration

- Record the date and time of the first puncture on the vial label.
- Novavax COVID-19 Vaccine, Adjuvanted is available in two presentations:
    - Multi-dose vial containing 5 doses of 0.5 mL each
    - Multi-dose vial containing 10 doses of 0.5 mL each
- Do not pool excess vaccine from multiple vials.
- After the first needle puncture, hold the vial between 2 to 25°C (36 to 77°F) for up to 6 hours.
- Discard vial 6 hours after the first puncture.

2.2 Administration

Administer the Novavax COVID-19 Vaccine, Adjuvanted intramuscularly.

2.3 Dosing and Schedule

Primary Series

The Novavax COVID-19 Vaccine, Adjuvanted is administered intramuscularly as a primary series of two doses (0.5 mL each) 3 weeks apart in individuals 12 years of age and older.

Booster Dose

A first booster dose (0.5 mL) of Novavax COVID-19 Vaccine, Adjuvanted may be administered intramuscularly at least 6 months after completion of primary vaccination with an authorized or approved COVID-19 vaccine to individuals 18 years of age and older for whom an FDA-authorized mRNA bivalent COVID-19 booster vaccine is not accessible or clinically appropriate and in individuals 18 years of age and older who elect to receive the Novavax COVID-19 Vaccine, Adjuvanted because they would otherwise not receive a booster dose of a COVID-19 vaccine.

3 DOSAGE FORMS AND STRENGTHS

The Novavax COVID-19 Vaccine, Adjuvanted is a suspension for injection. A single dose is 0.5 mL.

4 CONTRAINDICATIONS

Do not administer the Novavax COVID-19 Vaccine, Adjuvanted to individuals with a known history of severe allergic reaction (e.g., anaphylaxis) to any component of the Novavax COVID-19 Vaccine, Adjuvanted *[see Description (13)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Management of Acute Allergic Reactions

Appropriate medical treatment to manage immediate allergic reactions must be immediately available in the event an acute anaphylactic reaction occurs following administration of the Novavax COVID-19 Vaccine, Adjuvanted.

Monitor the Novavax COVID-19 Vaccine, Adjuvanted recipients for the occurrence of immediate adverse reactions according to the Centers for Disease Control and Prevention guidelines (https://www.cdc.gov/vaccines/covid-19/clinical-considerations/managing-anaphylaxis.html).

5.2 Myocarditis and Pericarditis

Clinical trials data provide evidence for increased risks of myocarditis and pericarditis following administration of Novavax COVID-19 Vaccine, Adjuvanted *[see Clinical Trials Experience (6.1)]*.

The CDC has published considerations related to myocarditis and pericarditis after vaccination, including for vaccination of individuals with a history of myocarditis or pericarditis (https://www.cdc.gov/vaccines/covid-19/clinical-considerations/interim-considerations-us.html#myocarditis-pericarditis).

5.3 Syncope

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

5.4 Altered Immunocompetence

Immunocompromised persons, including individuals receiving immunosuppressant therapy, may have a diminished immune response to the Novavax COVID-19 Vaccine, Adjuvanted.

5.5 Limitations of Vaccine Effectiveness

The Novavax COVID-19 Vaccine, Adjuvanted may not protect all vaccine recipients.

6 OVERALL SAFETY SUMMARY

It is MANDATORY for vaccination providers to report to the Vaccine Adverse Event Reporting System (VAERS) all vaccine administration errors, all serious adverse events, cases of myocarditis, cases of pericarditis, cases of Multisystem Inflammatory Syndrome (MIS) in adults and children, and hospitalized or fatal cases of COVID-19 following vaccination with the Novavax COVID-19 Vaccine, Adjuvanted. To the extent feasible, provide a copy of the VAERS form to Novavax, Inc. Please see the REQUIREMENTS AND INSTRUCTIONS FOR REPORTING ADVERSE EVENTS AND VACCINE ADMINISTRATION ERRORS section for details on reporting to VAERS and Novavax, Inc.

Adverse Reactions in Clinical Trials

Primary Series

In a clinical trial, among participants 18 through 64 years of age, solicited adverse reactions (ARs) following administration of any dose of the Novavax COVID-19 Vaccine, Adjuvanted were injection site pain/tenderness (82.2%), fatigue/malaise (62.0%), muscle pain (54.1%), headache (52.9%), joint pain (25.4%), nausea/vomiting (15.6%), injection site redness (7.0%), injection site swelling (6.3%), and fever (6.0%). In participants ≥ 65 years of age, solicited ARs following administration of any dose of the Novavax COVID-19 Vaccine, Adjuvanted were injection site pain/tenderness (63.4%), fatigue/malaise (39.2%), muscle pain (30.2%), headache (29.2%), joint pain (15.4%), nausea/vomiting (7.3%), injection site swelling (5.3%), injection site redness (4.8%), and fever (2.0%).

In a clinical trial, among participants 12 through 17 years of age, solicited ARs following administration of any dose of the Novavax COVID-19 Vaccine, Adjuvanted were injection site pain/tenderness (79.8%), headache (63.3%), fatigue/malaise (61.6%), muscle pain (56.9%), nausea/vomiting (23.1%), joint pain (19.5%), fever (16.7%), injection site swelling (8.5%), and injection site redness (7.7%).

Myocarditis, pericarditis, chills, injection site pruritus, hypersensitivity reactions, lymphadenopathy-related reactions, and decreased appetite have been reported following administration of the Novavax COVID-19 Vaccine, Adjuvanted.

Booster Dose

In a clinical trial, among participants 18 years of age and older, solicited ARs following administration of a booster dose of the Novavax COVID-19 Vaccine, Adjuvanted were injection site pain/tenderness (81.1%), fatigue/malaise (63.4%), muscle pain (63.0%), headache (52.9%), joint pain (30.3%), nausea/vomiting (14.7%), injection site swelling (8.4%), injection site redness (6.3%), and fever (6.3%).

6.1 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 with rates in the clinical trials of another vaccine and may not reflect the rates observed in practice.

Two-Dose Primary Series

Participants 18 years of age and older

Safety of the Novavax COVID-19 Vaccine, Adjuvanted was assessed in a clinical study conducted in the United States (US) and Mexico (NCT04611802; Study 1). In this study, 26,106 participants 18 years of age and older have received at least one dose of the Novavax COVID-19 Vaccine, Adjuvanted. Additional safety data are available from three other clinical trials in the United Kingdom (NCT04583995; Study 2), South Africa (NCT04533399; Study 3), and Australia (NCT04368988, Parts 1 and 2 in Australia and the US; Study 4) which evaluated a COVID-19 vaccine containing the SARS-CoV-2 recombinant spike (rS) protein and Matrix-M adjuvant but manufactured by a different process.

Adolescents 12 Through 17 Years of Age

Safety of the Novavax COVID-19 Vaccine, Adjuvanted in adolescents was assessed in the adolescent primary series expansion of Study 1 conducted in the US. In this study, 2,232 participants 12 through 17 years of age have received at least one dose of Novavax COVID-19 Vaccine, Adjuvanted (n=1,487) or placebo (n=745).

Safety Data from Study 1

In Study 1, an ongoing Phase 3, multicenter, randomized, observer-blinded, placebo-controlled study, participants 18 years of age and older have received the Novavax COVID-19 Vaccine, Adjuvanted (n=19,735) or placebo (n=9,847). Overall, 52.0% were male, 48.0% were female; 75.0% were White, 11.8% were Black or African American, 4.1% were Asian, 6.7% were American Indian (including Native Americans) or Alaskan Native, and 1.6% were multiple races; 21.9% were Hispanic/Latino. Demographic characteristics of participants were well balanced between the Novavax COVID-19 Vaccine, Adjuvanted and placebo groups. During the study, COVID-19 vaccines authorized for emergency use became available, and participants, when

eligible for vaccination, were offered the opportunity to cross over from the originally assigned study treatment to the other study treatment (vaccine or placebo) in a blinded fashion ("blinded crossover"). In the post-crossover period, 6,416 participants received the Novavax COVID-19 Vaccine, Adjuvanted, and 15,298 participants received placebo. The demographic characteristics of participants in the pre- and post-crossover groups were comparable. Due to data quality issues at two study sites, a total of 289 additional participants were excluded from the safety analysis set.

Study 1 also included an adolescent primary series expansion. In the pre-crossover period, among adolescent participants who received at least one dose of vaccine (n=1487) or placebo (n=745), 52.5% were male, 47.5% were female; 74.4% were White, 13.9% were Black or African American, 3.4% were Asian, 2.1% were American Indian (including Native Americans) or Alaskan Native, and 5.3% were multiple races; 18.5% were Hispanic/Latino. Demographic characteristics were well balanced between the Novavax COVID-19 Vaccine, Adjuvanted and placebo groups. During the study, COVID-19 vaccines authorized for emergency use became available, and participants, when eligible for vaccination, were offered the opportunity to cross over from the originally assigned study treatment to the other study treatment (vaccine or placebo) in a blinded fashion ("blinded crossover"). In the post-crossover period, 665 participants received the Novavax COVID-19 Vaccine, Adjuvanted, and 1,353 participants received placebo. The demographic characteristics of participants in the pre- and post-crossover groups were comparable.

Study 1 was amended to include a booster dose in which 12,738 individuals 18 to 96 years of age received a booster dose of the Novavax COVID-19 Vaccine, Adjuvanted starting approximately 6 months after the two-dose primary series.

Participants 18 years of age and older

Solicited Adverse Reactions

During the pre-crossover period, local and systemic adverse reactions were solicited within 7 days following each dose of the Novavax COVID-19 Vaccine, Adjuvanted or placebo in participants using an electronic diary.

The reported frequency and severity of solicited local and systemic adverse reactions series are presented for participants 18 through 64 years of age in Table 1.

Table 1 Number and Percentage of Participants with Solicited Local and Systemic Adverse Reactions Starting within 7 Days[a] After Each Dose in Participants 18-64 Years (Solicited Safety Set,[b] Dose 1 and Dose 2)[c]

Event	Novavax COVID-19 Vaccine, Adjuvanted		Placebo[d]	
	Primary Series		Primary Series	
	Dose 1 N = 15884 n (%)	Dose 2 N = 15148 n (%)	Dose 1 N = 7868 n (%)	Dose 2 N = 7361 n (%)
Local Adverse Reactions				
Pain/tenderness				
Any Grade	9604 (60.5)	12234 (80.8)	1706 (21.7)	1623 (22.0)
Grade 3[e,f]	174 (1.1)	951 (6.3)	17 (0.2)	20 (0.3)
Grade 4[g]	0	5 (0.03)	0	1 (0.01)
Redness (erythema)				
Any Grade	151 (1.0)	1040 (6.9)	21 (0.3)	26 (0.4)
Grade 3[h]	3 (0.02)	134 (0.9)	0	2 (0.03)
Swelling				
Any Grade	137 (0.9)	943 (6.2)	24 (0.3)	22 (0.3)
Grade 3[i]	7 (0.04)	82 (0.5)	3 (0.04)	1 (0.01)
Systemic Adverse Reactions				
Fever				
Any Grade	56 (0.4)	941 (6.2)	31 (0.4)	16 (0.2)
Grade 3[j]	7 (0.04)	60 (0.4)	7 (0.09)	2 (0.03)
Grade 4[k]	4 (0.03)	2 (0.01)	1 (0.01)	0
Headache				
Any Grade	4158 (26.2)	7128 (47.1)	1866 (23.7)	1492 (20.3)
Grade 3[l]	132 (0.8)	492 (3.2)	58 (0.7)	36 (0.5)
Grade 4[m]	4 (0.03)	5 (0.03)	1 (0.01)	2 (0.03)
Fatigue/malaise				
Any Grade	4892 (30.8)	8825 (58.3)	2095 (26.6)	1889 (25.7)
Grade 3[n]	249 (1.6)	1591 (10.5)	113 (1.4)	114 (1.5)
Grade 4[m]	8 (0.05)	7 (0.05)	1 (0.01)	3 (0.04)
Muscle pain (myalgia)				
Any Grade	3827 (24.1)	7682 (50.7)	1073 (13.6)	900 (12.2)
Grade 3[n]	79 (0.5)	805 (5.3)	31 (0.4)	28 (0.4)
Grade 4[m]	2 (0.01)	5 (0.03)	1 (0.01)	4 (0.05)
Joint pain (arthralgia)				
Any Grade	1260 (7.9)	3542 (23.4)	522 (6.6)	504 (6.8)
Grade 3[n]	49 (0.3)	393 (2.6)	25 (0.3)	22 (0.3)
Grade 4[m]	1 (< 0.01)	5 (0.03)	0	2 (0.03)

Table 1 Number and Percentage of Participants with Solicited Local and Systemic Adverse Reactions Starting within 7 Days[a] After Each Dose in Participants 18-64 Years (Solicited Safety Set,[b] Dose 1 and Dose 2)[c]

Event	Novavax COVID-19 Vaccine, Adjuvanted		Placebo[d]	
	Primary Series		Primary Series	
	Dose 1 N = 15884 n (%)	Dose 2 N = 15148 n (%)	Dose 1 N = 7868 n (%)	Dose 2 N = 7361 n (%)
Nausea or vomiting				
Any Grade	1069 (6.7)	1822 (12.0)	466 (5.9)	417 (5.7)
Grade 3[o]	18 (0.1)	26 (0.2)	7 (0.09)	7 (0.1)
Grade 4[p]	4 (0.03)	7 (0.05)	2 (0.03)	2 (0.03)

[a] 7 days included day of vaccination and the subsequent 6 days. Events and use of antipyretic or pain medication were collected in the electronic diary (eDiary).
[b] Solicited safety set includes participants who received at least one dose of study vaccine and completed their eDiary.
[c] Absence of rows for Grade 4 adverse reactions indicates no events were reported.
[d] Placebo was a saline solution.
[e] Grade 3 pain: Defined as any use of narcotic pain reliever or prevents daily activity.
[f] Grade 3 tenderness: Defined as significant discomfort at rest.
[g] Grade 4 pain/ tenderness: Defined as Emergency Room (ER) visit or hospitalization.
[h] Grade 3 redness (erythema): Defined as > 10 cm.
[i] Grade 3 swelling: Defined as > 10 cm or prevents daily activity.
[j] Grade 3 fever: Defined as 39.0 to 40°C (102.1 to 104°F).
[k] Grade 4 fever: Defined as > 40°C (> 104°F).
[l] Grade 3 headache: Defined as significant; any use of narcotic pain reliever or prevents daily activity.
[m] Grade 4 headache, fatigue/malaise, muscle pain (myalgia), joint pain (arthralgia): Defined as ER visit or hospitalization.
[n] Grade 3 fatigue/malaise, muscle pain (myalgia), joint pain (arthralgia): Defined as significant; prevents daily activity.
[o] Grade 3 nausea or vomiting: Defined as prevents daily activity, requires outpatient IV hydration.
[p] Grade 4 nausea or vomiting: Defined as ER visit or hospitalization for hypotensive shock.

The reported frequency and severity of solicited local and systemic adverse reactions are presented for participants 65 years of age and older in Table 2.

Table 2 Number and Percentage of Participants with Solicited Local and Systemic Adverse Reactions Starting within 7 Days[a] After Each Dose in Participants 65 Years and Older (Solicited Safety Set,[b] Dose 1 and Dose 2)[c]

Event	Novavax COVID-19 Vaccine, Adjuvanted		Placebo[d]	
	Primary Series		Primary Series	
	Dose 1 N = 2251 n (%)	Dose 2 N = 2048 n (%)	Dose 1 N = 1114 n (%)	Dose 2 N = 978 n (%)
Local Adverse Reactions				
Pain/tenderness				
Any Grade	854 (37.9)	1258 (61.4)	175 (15.7)	161 (16.5)
Grade 3[e,f]	13 (0.6)	43 (2.1)	3 (0.3)	1 (0.1)

Table 2 Number and Percentage of Participants with Solicited Local and Systemic Adverse Reactions Starting within 7 Days[a] After Each Dose in Participants 65 Years and Older (Solicited Safety Set,[b] Dose 1 and Dose 2)[c]

Event	Novavax COVID-19 Vaccine, Adjuvanted		Placebo[d]	
	Primary Series		Primary Series	
	Dose 1 N = 2251 n (%)	Dose 2 N = 2048 n (%)	Dose 1 N = 1114 n (%)	Dose 2 N = 978 n (%)
Redness (erythema)				
Any Grade	16 (0.7)	99 (4.8)	5 (0.4)	4 (0.4)
Grade 3[g]	0	7 (0.3)	0	0
Swelling				
Any Grade	18 (0.8)	111 (5.4)	1 (0.09)	4 (0.4)
Grade 3[h]	1 (0.04)	8 (0.4)	0	1 (0.1)
Systemic Adverse Reactions				
Fever				
Any Grade	8 (0.4)	40 (2.0)	3 (0.3)	7 (0.7)
Grade 3[i]	1 (0.04)	2 (0.1)	0	1 (0.1)
Headache				
Any Grade	344 (15.3)	502 (24.5)	184 (16.5)	144 (14.7)
Grade 3[j]	12 (0.5)	18 (0.9)	4 (0.4)	2 (0.2)
Grade 4[k]	1 (0.04)	1 (0.05)	0	0
Fatigue/malaise				
Any Grade	444 (19.7)	714 (34.9)	202 (18.1)	182 (18.6)
Grade 3[l]	23 (1.0)	68 (3.3)	5 (0.4)	13 (1.3)
Muscle pain (myalgia)				
Any Grade	284 (12.6)	561 (27.4)	125 (11.2)	102 (10.4)
Grade 3[l]	3 (0.1)	32 (1.6)	4 (0.4)	2 (0.2)
Joint pain (arthralgia)				
Any Grade	139 (6.2)	271 (13.2)	71 (6.4)	63 (6.4)
Grade 3[l]	4 (0.2)	16 (0.8)	4 (0.4)	2 (0.2)
Grade 4[k]	0	1 (0.05)	0	0
Nausea/vomiting				
Any Grade	81 (3.6)	108 (5.3)	32 (2.9)	35 (3.6)
Grade 3[m]	0	3 (0.1)	0	0

[a] 7 days included day of vaccination and the subsequent 6 days. Events and use of antipyretic or pain medication were collected in the electronic diary (eDiary).
[b] Solicited safety set includes participants who received at least one dose of study vaccine and completed their eDiary.
[c] Absence of rows for Grade 4 adverse reactions indicates no events were reported.
[d] Placebo was a saline solution.
[e] Grade 3 pain: Defined as any use of narcotic pain reliever or prevents daily activity.
[f] Grade 3 tenderness: Defined as significant discomfort at rest.
[g] Grade 3 redness (erythema): Defined as > 10 cm.
[h] Grade 3 swelling: Defined as > 10 cm or prevents daily activity.
[i] Grade 3 fever: Defined as 39.0 to 40°C (102.1 to 104°F).

[j] Grade 3 headache: Defined as significant; any use of narcotic pain reliever or prevents daily activity.
[k] Grade 4 headache, joint pain (arthralgia): Defined as ER visit or hospitalization.
[l] Grade 3 fatigue/malaise, muscle pain (myalgia), joint pain (arthralgia): Defined as significant; prevents daily activity.
[m] Grade 3 nausea or vomiting: Defined as prevents daily activity, requires outpatient IV hydration.

Unsolicited Adverse Events (non-serious and serious)

In Study 1, participants were monitored for non-serious unsolicited adverse events from the first dose through 28 days after the second dose in both the pre- and post-crossover periods and for serious adverse events for the duration of study participation. Participants who only received the first dose in the pre- and post-crossover periods were monitored for non-serious unsolicited adverse events through 49 days after administration of vaccine or placebo and for serious adverse events for the duration of study participation. In the pre-crossover period 19,735 participants received the Novavax COVID-19 Vaccine, Adjuvanted and 9,847 participants received placebo. In the post-crossover period, 6,416 participants received the Novavax COVID-19 Vaccine, Adjuvanted and 15,298 received placebo. Of participants who received two doses of the Novavax COVID-19 Vaccine, Adjuvanted in the pre-crossover period (n=19,111), 78% had a follow-up duration of at least 2 months (median = 2.5 months) after Dose 2. Of participants who received two doses of the Novavax COVID-19 Vaccine, Adjuvanted in the post-crossover period (n=6,346), 99% had a follow-up duration of at least 2 months (median = 4.4 months) after the last dose.

From Dose 1 through 28 days following Dose 2 in the pre-crossover period, the overall frequency of non-serious unsolicited adverse events was similar in the Novavax COVID-19 Vaccine, Adjuvanted group (11.6%) and the placebo group (11.2%). The most frequently reported unsolicited adverse reactions were chills (0.4% vaccine recipients vs. 0.1% placebo recipients), lymphadenopathy-related reactions (0.3% vaccine recipients vs. 0.1% placebo recipients), and injection site pruritus (0.1% vaccine recipients vs. 0.0% placebo recipients). Lymphadenopathy-related reactions included lymphadenopathy, lymphadenitis, lymph node pain, and axillary pain. All lymphadenopathy-related reactions occurred in participants 18 through 64 years of age.

In the pre-crossover period, serious adverse events were reported by 199 (1.0%) participants in the Novavax COVID-19 Vaccine, Adjuvanted group and by 108 (1.1%) participants in the placebo group. In the post-crossover period, serious adverse events were reported by 88 (1.4%) participants who received the Novavax COVID-19 Vaccine, Adjuvanted and by 178 (1.2%) participants who received placebo.

Within 7 days of any dose (including 26,151 Novavax COVID-19 Vaccine, Adjuvanted recipients and 25,145 placebo recipients in both the pre- and post-crossover periods), hypersensitivity reactions (including urticaria, hypersensitivity, angioedema, and swelling of the face, lips, ear, and/or eyelids) were reported by 26 participants after the Novavax COVID-19 Vaccine, Adjuvanted (0.1%) and 8 participants after placebo (0.03%). Of these events, 1 reaction (generalized urticaria and facial angioedema with a duration of 2 days) was serious and occurred 2 days after Dose 1 of the Novavax COVID-19 Vaccine, Adjuvanted.

Within 28 days of any dose, the following numerical imbalances with more events in vaccine than placebo recipients (including 26,151 Novavax COVID-19 Vaccine, Adjuvanted recipients

and 25,145 placebo recipients in both the pre- and post-crossover periods) were observed for the following serious and other adverse events of interest.

- Myocarditis and/or pericarditis were reported by two participants after the Novavax COVID-19 Vaccine, Adjuvanted (0.01%) and no participants after placebo. One serious event was reported by a 67-year-old male 28 days after Dose 1, associated with concomitant COVID-19, and one non-serious event was reported by a 20-year-old male 10 days after Dose 1. Among the two reported events, one was reported as resolved and one did not have follow-up available. Reports of myocarditis and/or pericarditis from Study 1 and Study 2 (see Safety Data from Study 2) provide evidence for increased risks of myocarditis and pericarditis following administration of the Novavax COVID-19 Vaccine, Adjuvanted.
- Events of cardiomyopathy or cardiac failure were reported by eight participants after the Novavax COVID-19 Vaccine, Adjuvanted (0.03%) and one participant after placebo (< 0.01%). All events were serious. Additionally, an event of congestive cardiac failure was reported after the Novavax COVID-19 Vaccine, Adjuvanted by a participant who was excluded from the safety analysis set. Currently available information on cardiomyopathy or cardiac failure is insufficient to determine a causal relationship with the vaccine.
- Events of acute cholecystitis were reported by six participants after the Novavax COVID-19 Vaccine, Adjuvanted (0.02%) and two participants after placebo (0.01%). All events were serious. Currently available information on cholecystitis is insufficient to determine a causal relationship with the vaccine.
- A total of 12 non-cardiac, non-neurovascular thrombotic and embolic events were reported by 11 participants after the Novavax COVID-19 Vaccine, Adjuvanted (0.04%) and a total of seven events were reported by six participants after placebo (0.02%). Events following the Novavax COVID-19 Vaccine, Adjuvanted included pulmonary embolism (n=5), deep vein thrombosis (n=2), thrombosis (n=2), and portal vein thrombosis, mesenteric artery thrombosis, and peripheral arterial occlusive disease (n=1 each); six of the events were serious, including pulmonary embolism (n=5) and deep vein thrombosis (n=1). Events following placebo included pulmonary embolism (n=3), and deep vein thrombosis and peripheral arterial occlusive disease (n=2 each), all of which were serious except deep vein thrombosis and peripheral arterial occlusive disease (n=1 each). Currently available information on non-cardiac, non-neurovascular thrombotic and embolic events is insufficient to determine a causal relationship with the vaccine.

Events of uveitis (iritis, uveitis, iridocyclitis) were reported by 3 participants after Novavax COVID-19 Vaccine, Adjuvanted (0.01%) and 2 participants after placebo (0.01%). All events were non-serious. One participant had onset of uveitis after Dose 1 of Novavax COVID-19 Vaccine, Adjuvanted which resolved and then recurred following Dose 2. The two placebo recipients with events appeared to have had a previous history of uveitis and one of the Novavax COVID-19 Vaccine, Adjuvanted recipients had a history of iritis. Currently available information on uveitis is insufficient to determine a causal relationship with the vaccine.

Adolescents 12 Through 17 Years of Age

Solicited Adverse Reactions

During the pre-crossover period, local and systemic adverse reactions were solicited within 7 days following each dose of the Novavax COVID-19 Vaccine, Adjuvanted or placebo in participants using an electronic diary.

The reported frequency and severity of solicited local and systemic adverse reactions are presented for participants 12 through 17 years of age in Table 3.

Table 3 Number and Percentage of Participants with Solicited Local and Systemic Adverse Reactions Starting within 7 Days[a] After Each Dose in Participants 12-17 Years (Solicited Safety Set,[b] Dose 1 and Dose 2)[c]

Event	Novavax COVID-19 Vaccine, Adjuvanted		Placebo[d]	
	Dose 1 N = 1448 n (%)	Dose 2 N = 1394 n (%)	Dose 1 N = 726 n (%)	Dose 2 N = 686 n (%)
Local Adverse Reactions				
Pain/tenderness				
Any Grade	945 (65.3)	1045 (75.0)	204 (28.1)	141 (20.6)
Grade 3[e,f]	22 (1.5)	108 (7.7)	4 (0.6)	4 (0.6)
Redness (erythema)				
Any Grade	15 (1.0)	104 (7.5)	5 (0.7)	0
Grade 3[g]	0	10 (0.7)	0	0
Swelling				
Any Grade	20 (1.4)	111 (8.0)	3 (0.4)	1 (0.1)
Grade 3[h]	0	8 (0.6)	1 (0.1)	0
Systemic Adverse Reactions				
Fever				
Any Grade	11 (0.8)	235 (16.9)	5 (0.7)	1 (0.1)
Grade 3[i]	1 (0.07)	31 (2.2)	0	0
Grade 4[j]	2 (0.1)	0	0	0
Headache				
Any Grade	440 (30.4)	793 (56.9)	181 (24.9)	119 (17.3)
Grade 3[k]	13 (0.9)	87 (6.2)	12 (1.7)	14 (2.0)
Grade 4[l]	0	1 (0.07)	0	0
Fatigue/malaise				
Any Grade	418 (28.9)	807 (57.9)	142 (19.6)	113 (16.5)
Grade 3[m]	33 (2.3)	223 (16.0)	13 (1.8)	13 (1.9)
Muscle pain (myalgia)				
Any Grade	492 (34.0)	683 (49.0)	114 (15.7)	82 (12.0)
Grade 3[m]	17 (1.2)	104 (7.5)	4 (0.6)	6 (0.9)

Table 3 Number and Percentage of Participants with Solicited Local and Systemic Adverse Reactions Starting within 7 Days[a] After Each Dose in Participants 12-17 Years (Solicited Safety Set,[b] Dose 1 and Dose 2)[c]

Event	Novavax COVID-19 Vaccine, Adjuvanted		Placebo[d]	
	Dose 1 N = 1448 n (%)	Dose 2 N = 1394 n (%)	Dose 1 N = 726 n (%)	Dose 2 N = 686 n (%)
Joint pain (arthralgia)				
Any Grade	102 (7.0)	226 (16.2)	35 (4.8)	21 (3.1)
Grade 3[m]	6 (0.4)	40 (2.9)	1 (0.1)	2 (0.3)
Nausea or vomiting				
Any Grade	113 (7.8)	277 (19.9)	56 (7.7)	33 (4.8)
Grade 3[n]	2 (0.1)	14 (1.0)	3 (0.4)	3 (0.4)
Grade 4[o]	0	1 (0.07)	0	0

[a] 7 days included day of vaccination and the subsequent 6 days. Events and use of antipyretic or pain medication were collected in the electronic diary (eDiary).
[b] Solicited safety set includes participants who received at least one dose of study vaccine and completed their eDiary.
[c] Absence of rows for Grade 4 adverse reactions indicates no events were reported.
[d] Placebo was a saline solution.
[e] Grade 3 pain: Defined as any use of narcotic pain reliever or prevents daily activity.
[f] Grade 3 tenderness: Defined as significant discomfort at rest.
[g] Grade 3 redness (erythema): Defined as > 10 cm.
[h] Grade 3 swelling: Defined as > 10 cm or prevents daily activity.
[i] Grade 3 fever: Defined as 39.0 to 40°C (102.1 to 104°F).
[j] Grade 4 fever: Defined as > 40°C (> 104°F).
[k] Grade 3 headache: Defined as significant; any use of narcotic pain reliever or prevents daily activity.
[l] Grade 4 headache, fatigue/malaise, muscle pain (myalgia), joint pain (arthralgia): Defined as ER visit or hospitalization.
[m] Grade 3 fatigue/malaise, muscle pain (myalgia), joint pain (arthralgia): Defined as significant; prevents daily activity.
[n] Grade 3 nausea or vomiting: Defined as prevents daily activity, requires outpatient IV hydration.
[o] Grade 4 nausea or vomiting: Defined as ER visit or hospitalization for hypotensive shock.

Unsolicited Adverse Events (non-serious and serious)

In Study 1, participants were monitored for non-serious unsolicited adverse events from the first dose through 28 days after the second dose in both the pre- and post-crossover periods and for serious adverse events for the duration of study participation. Participants who only received the first dose in the pre- and post-crossover periods were monitored for non-serious unsolicited adverse events through 49 days after administration of vaccine or placebo and for serious adverse events for the duration of study participation. In the pre-crossover period 1,487 participants received the Novavax COVID-19 Vaccine, Adjuvanted and 745 participants received placebo. In the post-crossover period, 665 participants received the Novavax COVID-19 Vaccine, Adjuvanted and 1,353 received placebo. Of participants who received two doses of the Novavax COVID-19 Vaccine, Adjuvanted in the pre-crossover period (n=1,468), 86% had a follow-up duration of at least 2 months (median = 71 days) after Dose 2. Of participants who received two doses of the Novavax COVID-19 Vaccine, Adjuvanted in the post-crossover period (n=638), 43% had a follow-up duration of at least 1 month (median = 30 days) after the last dose.

From Dose 1 through 28 days following Dose 2 in the pre-crossover period, the overall frequency of non-serious unsolicited adverse events was similar in the Novavax COVID-19 Vaccine,

Adjuvanted group (15.5%) and the placebo group (15.3%). The most frequently reported unsolicited adverse reactions were lymphadenopathy-related reactions (0.9% vaccine recipients vs. 0.0% placebo recipients), fatigue (0.5% vaccine recipients vs. 0.0% placebo recipients), decreased appetite (0.3% vaccine recipients vs. 0.0% placebo recipients), arthralgia (0.2% vaccine recipients vs. 0.0% placebo recipients), injection site pruritus (0.2% vaccine recipients vs. 0.0% placebo recipients), and myalgia (0.1% vaccine recipients vs. 0.0% placebo recipients). Lymphadenopathy-related reactions included lymphadenopathy, lymph node pain, and axillary pain.

In the pre-crossover period, serious adverse events were reported by 7 (0.5%) participants in the Novavax COVID-19 Vaccine, Adjuvanted group and by 2 (0.3%) participants in the placebo group. In the post-crossover period, serious adverse events were reported by 3 (0.5%) participants who received the Novavax COVID-19 Vaccine, Adjuvanted and by 2 (0.1%) participants who received placebo.

Within 28 days of any dose, one serious adverse event of interest of myocarditis was observed. The event was reported by a 16-year-old adolescent participant 2 days after Dose 2 of the Novavax COVID-19 Vaccine, Adjuvanted.

Safety Data from Other Studies with Primary Series

Study 2 was a randomized, placebo-controlled study that included a crossover design. Approximately 10,800 participants received at least one dose of a COVID-19 vaccine containing SARS-CoV-2 recombinant spike (rS) protein and Matrix-M adjuvant, manufactured by a different process than the Novavax COVID-19 Vaccine, Adjuvanted evaluated in Study 1, and approximately 10,900 participants received at least one dose of placebo.

Serious events of myocarditis in a 19-year-old male and pericarditis in a 60-year-old female were reported within 10 days following administration of Dose 2 and Dose 1, respectively, of the vaccine. Both events were reported as resolved. No events of myocarditis or pericarditis were reported following administration of placebo.

A serious event of Guillain Barré syndrome was reported 9 days following administration of Dose 1 of the vaccine. No events of Guillain Barré syndrome were reported following administration of placebo.

In Studies 3 and 4, approximately 5,500 participants received at least one dose of a COVID-19 vaccine containing SARS-CoV-2 recombinant spike (rS) protein and Matrix-M adjuvant, manufactured by a different process than the Novavax COVID-19 Vaccine, Adjuvanted evaluated in Study 1. No serious adverse events considered related to vaccination were reported in these studies. No events of myocarditis/pericarditis or Guillain Barré syndrome were reported in vaccine recipients in these studies.

Booster Dose Following a Primary Series of Novavax COVID-19 Vaccine, Adjuvanted in Participants 18 Years or Older

In an open label portion of Study 1, 12,738 participants 18 years of age and older (based on enrollment until March 26, 2022) received a single booster dose of Novavax COVID-19 Vaccine, Adjuvanted (0.5 mL) at least 6 months after the two-dose primary series (median of 11.0 months between completion of primary series and booster dose). Safety analyses included evaluation of solicited local and systemic adverse reactions within 7 days after a booster dose (n=238) and nonserious unsolicited adverse events within 28 days after a booster dose (n=298). Safety analysis also included evaluation of serious adverse events and adverse events of interest after a booster dose (n=12,738) with a median follow-up of 121 days post booster dose through data extraction of August 18, 2022. The safety follow-up is ongoing.

Among the 12,738 boosted participants, 84.3% were between 18 and 64 years of age and 15.7% were 65 years of age and older, 50.6% were male, 49.4% were female; 72.6% were White, 14.4% were Black or African American, 3.8% were Asian, 6.5% were American Indian (including Native Americans) or Alaskan Native, 0.2% were Native Hawaiian or Other Pacific Islander, and 1.7% were multiple races; 21.4% were Hispanic or Latino.

Solicited Adverse Reactions

Local and systemic adverse reactions were solicited within 7 days following the third (booster) dose of the Novavax COVID-19 Vaccine, Adjuvanted using an electronic diary.

The reported frequency and severity of solicited local and systemic adverse reactions in participants 18 years of age and older are presented in Table 4.

Table 4 Number and Percentage of Participants with Solicited Local and Systemic Adverse Reactions Starting within 7[a] Days After Booster Dose in Participants 18 Years and Older (Booster Safety Analysis Set [b]) [c]

Event	Novavax COVID-19 Vaccine, Adjuvanted Booster N = 238 n (%)
Local Adverse Reactions	
Pain/tenderness	
Any Grade	193 (81.1)
Grade 3[d,e]	18 (7.6)
Redness (erythema)	
Any Grade	15 (6.3)
Grade 3[f]	1 (0.4)
Swelling	
Any Grade	20 (8.4)
Grade 3[g]	2 (0.8)

Table 4 Number and Percentage of Participants with Solicited Local and Systemic Adverse Reactions Starting within 7[a] Days After Booster Dose in Participants 18 Years and Older (Booster Safety Analysis Set [b]) [c]

Event	Novavax COVID-19 Vaccine, Adjuvanted Booster N = 238 n (%)
Systemic Adverse Reactions	
Fever	
Any Grade	15 (6.3)
Grade 3[h]	2 (0.8)
Headache	
Any Grade	126 (52.9)
Grade 3[i]	14 (5.9)
Fatigue/malaise	
Any Grade	151 (63.4)
Grade 3[j]	41 (17.2)
Grade 4[k]	2 (0.8)
Muscle pain (myalgia)	
Any Grade	150 (63.0)
Grade 3[j]	20 (8.4)
Grade 4[k]	2 (0.8)
Joint pain (arthralgia)	
Any Grade	72 (30.3)
Grade 3[j]	9 (3.8)
Nausea or vomiting	
Any Grade	35 (14.7)
Grade 3[l]	2 (0.8)
Grade 4[m]	1 (0.4)

[a] 7 days included day of vaccination and the subsequent 6 days. Events and use of antipyretic or pain medication were collected in the electronic diary (eDiary).
[b] The analysis included a total of 238 participants who received the booster dose who completed their eDiary
[c] Absence of rows for Grade 4 adverse reactions indicates no events were reported.
[d] Grade 3 pain: Defined as any use of narcotic pain reliever or prevents daily activity.
[e] Grade 3 tenderness: Defined as significant discomfort at rest.
[f] Grade 3 redness (erythema): Defined as > 10 cm.
[g] Grade 3 swelling: Defined as > 10 cm or prevents daily activity.
[h] Grade 3 fever: Defined as 39.0 to 40°C (102.1 to 104°F).
[i] Grade 3 headache: Defined as significant; any use of narcotic pain reliever or prevents daily activity.
[j] Grade 3 fatigue/malaise, muscle pain (myalgia), joint pain (arthralgia): Defined as significant; prevents daily activity.
[k] Grade 4 fatigue/malaise, muscle pain (myalgia): Defined as ER visit or hospitalization.
[l] Grade 3 nausea or vomiting: Defined as prevents daily activity, requires outpatient IV hydration.
[m] Grade 4 nausea or vomiting: Defined as ER visit or hospitalization for hypotensive shock.

Unsolicited Adverse Events (non-serious and serious)

Participants were monitored through 28 days after the booster dose for unsolicited adverse events. Out of 12,738 total booster participants, data are available for 298 participants for non-serious unsolicited adverse events until May 19, 2022 (median follow-up post booster of 122 days). There were no unsolicited adverse events that occurred in more than one participant.

Additionally, data for serious adverse events and adverse events of interest, including but not limited to allergic, neurologic, inflammatory, vascular, and autoimmune disorders, are available for 12,738 participants until August 18, 2022 (median follow-up post booster of 121 days).

An event of myocarditis was reported by a 28-year-old male participant 3 days after a booster dose of Novavax COVID-19 Vaccine, Adjuvanted in Study 1. The event following the booster dose was adjudicated as a non-ST elevation myocardial infarction; however, clinical features were also consistent with myocarditis (chest pain and elevated troponin), and no cardiac catheterization or cardiac MRI was performed during the acute presentation.

A serious adverse event of autoimmune hepatitis was reported in a 57-year-old male participant approximately 12 days after a booster dose of Novavax COVID-19 Vaccine, Adjuvanted. A year prior to vaccination, the participant had transient increases in alanine transferase (ALT), up to 3 times the upper limit of normal (ULN). From a normal baseline ALT prior to receipt of the first dose of Novavax COVID-19 Vaccine, Adjuvanted, ALT increased to 4 times ULN following the second dose of the primary series. After the booster dose, a recurrent and higher ALT increase was observed (7 times ULN). Viral hepatitis tests were negative, and no alternative etiologies have been identified. The event has been ongoing for 8 months and is not resolved with azathioprine treatment. Currently available information for this event is insufficient to determine a causal relationship with the vaccine.

Two serious adverse events in the injected arm were reported, including muscle edema in a 51-year-old female with onset 7 days after booster vaccination and cellulitis of the injection site in a 58-year-old male with onset 3 days after booster vaccination. The cellulitis resolved following antibiotic and steroid treatment. The muscle edema was not responsive to non-steroidal anti-inflammatory agents and has been ongoing for 6 months and is not resolved. Available information for these events is insufficient to determine a causal relationship with the vaccine.

A serious adverse event of extensive left leg and pelvic deep vein thrombosis and pulmonary embolism was reported 7 and 10 days, respectively, post booster in a 35-year-old female participant receiving oral contraceptive therapy. She required surgical intervention, thrombolytic therapy, and needs prolonged anti-coagulation. Available information for these events is insufficient to determine a causal relationship with the vaccine.

Booster Dose Following Primary Vaccination with Another Authorized or Approved COVID-19 Vaccine

The safety of a Novavax COVID-19 Vaccine, Adjuvanted booster dose in individuals who completed a primary vaccination with another authorized or approved COVID-19 vaccine (heterologous booster dose) is inferred from the report of an independent, multicenter, randomized, controlled, Phase 2, trial conducted in the United Kingdom (ISRCTN 73765130). This study was conducted in adults aged 30 years and older with no history of laboratory-confirmed SARS-CoV-2 infection. One study group (n=114 participants; median age 63 years) received Novavax COVID-19 Vaccine, Adjuvanted administered at least 84 days (median 105 days) after completion of the Pfizer-BioNTech COVID-19 Vaccine primary series. Reported adverse reactions through 28 days following a Novavax COVID-19 Vaccine, Adjuvanted booster dose did not identify any new safety concerns, as compared with adverse reactions reported following two doses of Novavax COVID-19 Vaccine, Adjuvanted given as a primary series.

6.2 Post-Authorization Experience

The following adverse reactions have been identified during post-authorization use of the Novavax COVID-19 Vaccine, Adjuvanted. Because these reactions are reported voluntarily, it is not always possible to reliably estimate their frequency or establish a causal relationship to vaccine exposure.

Cardiac Disorders: myocarditis, pericarditis

Immune System Disorders: anaphylaxis

Nervous System Disorders: paresthesia, hypoesthesia

8 REQUIREMENTS AND INSTRUCTIONS FOR REPORTING ADVERSE EVENTS AND VACCINE ADMINISTRATION ERRORS

See Overall Safety Summary (Section 6) for additional information.

The vaccination provider enrolled in the federal COVID-19 Vaccination Program is responsible for MANDATORY reporting of the listed events following the Novavax COVID-19 Vaccine, Adjuvanted to the Vaccine Adverse Event Reporting System (VAERS):

- Vaccine administration errors whether or not associated with an adverse event
- Serious adverse events* (irrespective of attribution to vaccination)
- Cases of myocarditis,
- Cases of pericarditis,
- Cases of Multisystem Inflammatory Syndrome (MIS) in adults and children
- Cases of COVID-19 that result in hospitalization or death

*Serious adverse events are defined as:

- Death;
- A life-threatening adverse event;
- Inpatient hospitalization or prolongation of existing hospitalization;
- A persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions;
- A congenital anomaly/birth defect;
- An important medical event that based on appropriate medical judgment may jeopardize the individual and may require medical or surgical intervention to prevent one of the outcomes listed above.

Instructions for Reporting to VAERS

The vaccination provider enrolled in the federal COVID-19 Vaccination Program should complete and submit a VAERS form to FDA using one of the following methods:

- Complete and submit the report online: https://vaers.hhs.gov/reportevent.html, or
- If you are unable to submit this form electronically, you may fax it to VAERS at 1-877-721-0366. If you need additional help submitting a report, you may call the VAERS toll-free information line at 1-800-822-7967 or send an email to info@vaers.org.

IMPORTANT: When reporting adverse events or vaccine administration errors to VAERS, please complete the entire form with detailed information. It is important that the information reported to the FDA be as detailed and as complete as possible. Information to include:

- Patient demographics (e.g., patient name, date of birth)
- Pertinent medical history
- Pertinent details regarding admission and course of illness
- Concomitant medications
- Timing of adverse event(s) in relationship to administration of the Novavax COVID-19 Vaccine, Adjuvanted
- Pertinent laboratory and virology information
- Outcome of the event and any additional follow-up information if it is available at the time of the VAERS report. Subsequent reporting of follow-up information should be completed if additional details become available.

The following steps are highlighted to provide the necessary information for safety tracking:

1. In Box 17, provide information on the Novavax COVID-19 Vaccine, Adjuvanted and any other vaccines administered on the same day; and in Box 22, provide information on any other vaccines received within one month prior.

2. In Box 18, description of the event:

    a. Write “Novavax COVID-19 Vaccine, Adjuvanted EUA” as the first line.

    b. Provide a detailed report of vaccine administration error and/or adverse event. It is important to provide detailed information regarding the patient and adverse event/medication error for ongoing safety evaluation of this unapproved vaccine. Please see information to include listed above.

3. Contact information:

    a. In Box 13, provide the name and contact information of the prescribing healthcare provider or institutional designee who is responsible for the report.

    b. In Box 14, provide the name and contact information of the best doctor/healthcare professional to contact about the adverse event.

    c. In Box 15, provide the address of the facility where vaccine was given (NOT the healthcare provider’s office address).

Other Reporting Instructions

Vaccination providers may report to VAERS other adverse events that are not required to be reported using the contact information above.

To the extent feasible, report adverse events to Novavax, Inc. using the contact information below or by providing a copy of the VAERS form to Novavax, Inc.

Website	Fax number	Telephone number
www.NovavaxMedInfo.com	1-888-988-8809	1-844-NOVAVAX (1-844-668-2829)

10 DRUG INTERACTIONS

There is no information on co-administration of the Novavax COVID-19 Vaccine, Adjuvanted with other vaccines.

11 USE IN SPECIFIC POPULATIONS

11.1 Pregnancy

Pregnancy Exposure Registry

There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to the Novavax COVID-19 Vaccine, Adjuvanted during pregnancy. Women who are vaccinated

with the Novavax COVID-19 Vaccine, Adjuvanted during pregnancy are encouraged to enroll in the registry by visiting https://c-viper.pregistry.com/.

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 miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively. Available data on the Novavax COVID-19 Vaccine, Adjuvanted administered to pregnant women are insufficient to inform vaccine-associated risks in pregnancy.

In a developmental toxicity study, 0.1 mL of a vaccine formulation containing the same quantity of SARS-CoV-2 rS protein (5 mcg), one-fifth the quantity of adjuvant (10 mcg) and inactive ingredients which comprise the formulation buffer (25 mM sodium phosphate, 300 mM sodium chloride, and 0.01% (w/v) polysorbate 80) contained in a single dose of the Novavax COVID-19 Vaccine, Adjuvanted was administered to female rats by the intramuscular route on four occasions: 27 and 13 days prior to mating, and on gestational days 7 and 15. No vaccine-related adverse effects on female fertility, fetal development or postnatal development were reported in the study.

11.2 Lactation

Risk Summary

Data are not available to assess the effects of the Novavax COVID-19 Vaccine, Adjuvanted on the breastfed infant or on milk production/excretion.

11.3 Pediatric Use

Emergency Use Authorization of Novavax COVID-19 Vaccine, Adjuvanted in adolescents 12 through 17 years of age is based on safety and effectiveness data in this age group and in adults.

The Novavax COVID-19 Vaccine, Adjuvanted is not authorized for use in individuals younger than 12 years of age.

11.4 Geriatric Use

Clinical studies that evaluated primary vaccination with the Novavax COVID-19 Vaccine, Adjuvanted included participants 65 years of age and older receiving vaccine or placebo, and their data contribute to the overall assessment of safety and efficacy. In an ongoing Phase 3 clinical study (Study 1), 12.6% (n=2,480 Novavax COVID-19 Vaccine, Adjuvanted, n=1,235 placebo) of participants were 65 years of age and older and 1.8% (n=361 Novavax COVID-19 Vaccine, Adjuvanted, n=179 placebo) of participants were 75 years of age and older. Vaccine efficacy in participants 65 years of age and older was 78.6% (95% CI: -16.6%, 96.1%) relative to 90.7% (95% CI: 72.9%, 96.8%) in participants 50 through 64 years of age. *[see Clinical Trial Results and Supporting Data for EUA (18)]*. Overall, there were no notable differences in the safety profiles observed between participants 65 years of age and older and younger participants. *[see Overall Safety Summary (6)]*

In the clinical study that evaluated a booster dose of Novavax COVID-19 Vaccine, Adjuvanted, 15.7% (n=2006) of participants were 65 years of age and older and 2.6% (n=326) of participants were 75 years of age and older. Overall, there were no notable differences in the safety profiles observed between participants 65 years of age and older and younger participants. *[see Overall Safety Summary (6)]*

13 DESCRIPTION

The Novavax COVID-19 Vaccine, Adjuvanted is a colorless-to-slightly yellow, clear-to-mildly opalescent suspension for intramuscular injection that is free from visible particles. Each 0.5 mL dose of the Novavax COVID-19 Vaccine, Adjuvanted contains 5 mcg of SARS-CoV-2 recombinant spike (rS) protein and 50 mcg Matrix-M adjuvant. The Matrix-M adjuvant is composed of Fraction-A (42.5 mcg) and Fraction-C (7.5 mcg) of saponin extracts from the soapbark tree, *Quillaja saponaria* Molina.

The rS protein is produced by recombinant DNA technology using a baculovirus expression system in an insect cell line that is derived from Sf9 cells of the *Spodoptera frugiperda* species.

Each dose of the Novavax COVID-19 Vaccine, Adjuvanted also contains the following ingredients: cholesterol, phosphatidylcholine, potassium dihydrogen phosphate (3.85 mcg), potassium chloride (2.25 mcg), disodium hydrogen phosphate dihydrate (14.7 mcg), disodium hydrogen phosphate heptahydrate (2.465 mg), sodium dihydrogen phosphate monohydrate (0.445 mg), sodium chloride (8.766 mg) and polysorbate 80 (0.050 mg), and Water for Injection. The pH is adjusted with sodium hydroxide or hydrochloric acid.

Each 0.5 mL dose of the Novavax COVID-19 Vaccine, Adjuvanted may also contain residual amounts of baculovirus and Sf9 cell proteins (≤ 0.96 mcg), baculovirus and cellular DNA (≤ 0.00016 mcg), lentil lectin (< 0.025 mcg), methyl-α-D-mannopyranoside (2 mcg), simethicone (< 0.92 mcg), pluronic F-68 (< 2.19 mcg), Triton X-100 (< 0.025 mcg), and Tergitol (NP9) (< 0.05 mcg).

The Novavax COVID-19 Vaccine, Adjuvanted does not contain preservative.

The vial stoppers are not made with natural rubber latex.

14 CLINICAL PHARMACOLOGY

14.1 Mechanism of Action

The Novavax COVID-19 Vaccine, Adjuvanted contains purified, full-length rS protein. The vaccine elicits an immune response to the rS protein, which protects against COVID-19.

18 CLINICAL TRIAL RESULTS AND SUPPORTING DATA FOR EUA

18.1 Efficacy of Two-Dose Primary Series in Participants 18 Years of Age and Older

Study 1 is an ongoing Phase 3, multicenter, randomized, observer-blinded, placebo-controlled study in participants 18 years of age and older in United States and Mexico.

Upon enrollment, participants were stratified by age (18 through 64 years or 65 years of age and older). The study excluded participants who were significantly immunocompromised due to immunodeficiency disease; had active cancer on chemotherapy; received chronic immunosuppressive therapy or received immunoglobulin or blood-derived products within 90 days; were pregnant or breastfeeding; or had a history of laboratory-confirmed diagnosed COVID-19. Participants with clinically stable underlying comorbidities were included as were participants with well-controlled human immunodeficiency virus (HIV) infection.

A total of 29,945 participants were randomized in a 2:1 ratio to receive two doses of the Novavax COVID-19 Vaccine, Adjuvanted or placebo 3 weeks apart. Assessments of safety and efficacy against COVID-19 are planned for up to 24 months after the second dose.

The primary efficacy analysis population (Per Protocol Efficacy [PP-EFF] Analysis Set) included 25,657 participants who received either the Novavax COVID-19 Vaccine, Adjuvanted (n=17,272) or placebo (n=8,385), received two doses (Dose 1 on day 0; Dose 2 on day 21 median 21 days, range 14-60), did not experience an exclusionary protocol deviation, and did not have evidence of SARS-CoV-2 infection through 6 days after the second dose. In the PP-EFF Analysis Set, 48.5% were female; 21.5% were Hispanic or Latino; 75.9% were White, 11.0% were Black or African American, 6.2% were American Indian or Alaska Native, 4.4% were Asian, and 1.7% were multiracial. The median age of participants was 47 years (range 18-95 years) and 11.7% were 65 years of age and older. Of the study participants in the PP-EFF Analysis Set, 95.2% were at high risk for COVID-19 due to living or working conditions involving known frequent exposure to SARS-CoV-2, comorbidities (chronic lung disease, cardiovascular disease, chronic liver disease, severe obesity, and diabetes), or age ≥ 65 years. Between participants who received the Novavax COVID-19 Vaccine, Adjuvanted and those who received placebo, there were no notable differences in demographics or pre-existing medical conditions. Participants in the PP-EFF Analysis Set were included in the primary efficacy analysis up until the time that they received their crossover vaccination. As of the September 27, 2021, data cutoff date, the PP-EFF Analysis Set had a median follow-up of 2.5 months post-Dose 2 during the pre-crossover period.

Efficacy of a Primary Series in Participants 18 Years of Age and Older

Vaccine efficacy in participants without evidence of SARS-CoV-2 infection through 6 days after the second dose is presented in Table 5. Based on data accrued through September 27, 2021, the efficacy of the Novavax COVID-19 Vaccine, Adjuvanted to prevent polymerase chain reaction (PCR)-confirmed symptomatic mild, moderate or severe COVID-19 from 7 days after Dose 2 was 90.4% (95% CI: 83.8%, 94.3%). In the PP-EFF Analysis Set, no cases of moderate or severe COVID-19 were reported in participants who had received the Novavax COVID-19 Vaccine, Adjuvanted, compared with nine cases of moderate COVID-19 and four cases of severe COVID-19 reported in participants who had received placebo.

Table 5 Vaccine Efficacy Against PCR-confirmed COVID-19 with Onset from 7 Days After Second Vaccination [1] (PP-EFF Analysis Set)

Subgroup	Novavax COVID-19 Vaccine, Adjuvanted			Placebo			Vaccine Efficacy (95% CI) (%)
	Participants N	COVID-19 Cases n (%)	Mean Incidence Rate Per 1,000 Person-Years[2]	Participants N	COVID-19 Cases n (%)	Mean Incidence Rate Per 1,000 Person-Years[2]	
Primary efficacy endpoint							
All participants	17,272	17 (0.1)	5.59	8,385	79 (0.9)	58.30	90.4 (83.8, 94.3) [3,4]
Mild	-	17 (0.1)	-	-	66 (0.8)	-	-
Moderate	-	0	-	-	9 (0.1)	-	-
Severe	-	0	-	-	4 (< 0.1)	-	-

[1] Vaccine efficacy (VE) evaluated in participants without major protocol deviations who are seronegative (for SARS-CoV-2) at baseline and do not have a laboratory confirmed current SARS-CoV-2 infection with symptom onset through 6 days after the second dose, and who have received two doses of vaccine or placebo as randomized.

[2] Mean incidence rate per 1,000 person-years was estimated with weighting for age strata reflective of the distribution seen in the study population.

[3] Based on log-linear model of PCR-confirmed COVID-19 infection incidence rate using Poisson regression with treatment group and age strata as fixed effects and robust error variance, where VE = 100 × (1 – ratio of incidence rate) (Zou 2004).

[4] Met primary efficacy endpoint criterion for success with a lower bound confidence interval (LBCI) > 30% at the planned primary confirmatory analysis.

Descriptive analyses of efficacy showed efficacy point estimates similar to the estimate for the overall study population across genders and racial groups, and across participants with or without medical comorbidities associated with high risk of severe COVID-19. Vaccine efficacy in participants of Hispanic/Latino ethnicity was 77.0% (95% CI: 48.7%, 89.7%) relative to 94.2% (95% CI: 87.9%, 97.2%) in participants who were not Hispanic/Latino. Vaccine efficacy in participants 65 years of age and older was 78.6% (95% CI: -16.6%, 96.1%) relative to 90.7% (95% CI: 72.9%, 96.8%) in participants 50 through 64 years of age.

18.2 Effectiveness of a Two-Dose Primary Series in Adolescents 12 Through 17 Years of Age

Effectiveness in adolescents 12 years through 17 years of age is based on a comparison of immune responses in this age group to adults 18 years through 25 years of age.

Study 1 is an ongoing Phase 3 multicenter, randomized, observer-blinded, placebo-controlled study that included 2,247 participants 12 through 17 years of age in the United States. Participants were randomized in a 2:1 ratio to receive two doses of the Novavax COVID-19 Vaccine, Adjuvanted or placebo 3 weeks apart. The study excluded participants who were significantly immunocompromised due to immunodeficiency disease; had active cancer on chemotherapy; had received chronic immunosuppressive therapy or had received immunoglobulin or blood-derived products within 90 days; were pregnant or breastfeeding; or had a history of laboratory-confirmed diagnosed COVID-19. Participants with clinically stable underlying comorbidities and participants with well-controlled HIV infection were included.

In Study 1, an analysis was conducted of SARS-CoV-2 neutralizing antibody titers 14 days after Dose 2 in a subset of adolescents 12 through 17 years of age and participants 18 through 25 years of age from the adult main study. Noninferior immune responses as assessed by geometric mean titers and seroconversion rates were demonstrated in a comparison of adolescents 12 through 17 years of age to participants 18 through 25 years of age (Table 6).

Table 6 SARS-CoV-2 Neutralizing Antibody Geometric Mean Titer Ratio and Seroconversion Rate – Comparison of Adolescents 12 Years Through 17 Years of Age to Participants 18 Years Through 25 Years of Age – Per-Protocol Immunogenicity Analysis Set

Assay	Time Point	12 Years Through 17 Years	18 Years Through 25 Years	12 Years Through 17 Years/ 18 Years Through 25 Years	
		GMT[a] (95% CI) n=390	**GMT[a] (95% CI) n=415**	**GMR[b] (95% CI)**	**Met Noninferiority Criteria[c]**
SARS-CoV-2 wild-type microneutralization assay (1/dilution)[d]	14 days after Dose 2	3859.6 (3422.8, 4352.1)	2611.8 (2367.4, 2881.5)	1.47 (1.26, 1.72)[3]	Yes
		SCR%[e] (95% CI) n=385	**SCR%[e] (95% CI) n=414**	**Difference in SCR%[f] (95% CI)**	
		98.7 (97.0, 99.6)	99.8 (98.7, 100.0)	-1.04 (-2.75, 0.20)	

CI = Confidence interval; GMR = Geometric mean ratio; GMT = Geometric mean titer; SCR = Seroconversion rate

[a] The 95% CI for GMT is calculated based on the t-distribution of the log-transformed values, then back transformed to the original scale for presentation.

[b] GMR is defined as the ratio of two geometric mean titers for comparison of two age cohorts. An analysis of covariance (ANCOVA) with age cohort as main effect and baseline microneutralization assay neutralizing antibodies as covariate was performed to estimate the GMR.

[c] Noninferiority was achieved if the following 3 pre-specified criteria were met simultaneously: 1) Lower bound of two-sided 95% CI for the ratio of GMTs ($GMT_{12\text{-}17yo}/GMT_{18\text{-}25yo}$) > 0.67; 2) Point estimate of the ratio of GMTs ≥ 0.82; and 3) Lower bound of the two-sided 95% CI for difference of SCRs ($SCR_{12\text{-}17yo}$ - $SCR_{18\text{-}25yo}$) was > -10%.

[d] Validated virus neutralizing assay (VNA) with wild-type virus (SARS-CoV-2 hCoV-19/Australia/VIC01/2020 [GenBank MT007544.1]; 360biolabs, Melbourne, Australia). The lower limit for quantification for this assay was a titer of 20, with titers below this level documented as 10.

[e] SCR is defined as percentage of participants with a ≥ 4-fold difference in titers between Day 35 and Day 0. The 95% CI for SCR was calculated using the Clopper-Pearson exact method.

[f] Difference in SCR in the adolescent primary series expansion (Study 1) for 12 years through 17 years of Study 1 minus SCR in Adult Main Study (Study 1) for 18 years through 25 years. The 95% CI for the difference of SCR between groups was calculated with the method of Miettinen and Nurminen.

A descriptive efficacy analysis evaluating PCR-confirmed symptomatic mild, moderate or severe COVID-19 cases was performed in 1,799 participants who were included in the per-protocol efficacy (PP-EFF) Analysis Set, which required receipt of two doses (Dose 1 on day 0; Dose 2 on day 21), no exclusionary protocol deviation(s), and no evidence of SARS-CoV-2 infection through 6 days after the second dose. In the PP-EFF Analysis Set, 47.2% were female; 15.8% were Hispanic or Latino; 76.1% were White, 12.9% were Black or African American, 1.1% were American Indian or Alaska Native, 3.6% were Asian, and 5.6% were multiracial. The median age of participants was 14 years (range 12-17 years). Of the study participants in the PP-EFF Analysis Set, 25.3% were obese. Between participants who received the Novavax COVID-19 Vaccine, Adjuvanted and those who received placebo, there were no notable differences in demographics. The median interval between doses of study vaccine was 22 days (range 14-43).

As of the August 9, 2021, data cutoff date, the PP-EFF Analysis Set had a median follow-up of 67 days post-Dose 2 during the pre-crossover period.

Vaccine efficacy in participants without evidence of SARS-CoV-2 infection through 6 days after the second dose is presented in Table 7 Based on data accrued through August 9, 2021, the efficacy of the Novavax COVID-19 Vaccine, Adjuvanted to prevent PCR-confirmed symptomatic mild, moderate or severe COVID-19 from 7 days after Dose 2 was 78.29% (95% CI: 37.55%, 92.45%). No cases of moderate or severe COVID-19 were reported in participants who had received the Novavax COVID-19 Vaccine, Adjuvanted or placebo.

Table 7 Vaccine Efficacy Against PCR-confirmed COVID-19 with Onset from 7 Days After Second Vaccination[1] (PP-EFF Analysis Set)

Subgroup	Novavax COVID-19 Vaccine, Adjuvanted			Placebo			Vaccine Efficacy (95% CI) (%)
	Partici-pants N	COVID-19 Cases[3] n (%)	Mean Incidence Rate Per 100 Person-Years	Partici-pants N	COVID-19 Cases[3] n (%)	Mean Incidence Rate Per 100 Person-Years	
Primary efficacy endpoint							
All participants	1205	5 (0.4)	2.69	594	11 (1.9)	12.38	78.29 (37.55, 92.45)[2]
Mild	-	5 (0.4)	-	-	11 (1.9)	-	-
Moderate	-	0	-	-	0	-	-
Severe	-	0	-	-	0	-	-

[1] Vaccine efficacy (VE) evaluated in participants without major protocol deviations who were seronegative (for SARS-CoV-2) at baseline and did not have a laboratory confirmed current SARS-CoV-2 infection with symptom onset through 6 days after the second dose, and who had received two doses of vaccine or placebo as randomized.

[2] Based on Modified Poisson regression with logarithmic link function and treatment group as fixed effect and robust error variance (Zou 2004).

[3] All cases for which sequence data are available (vaccine n=2; placebo n=7) were due to the Delta variant.

18.3 Immunogenicity of a Booster Dose Following a Novavax COVID-19 Vaccine, Adjuvanted Primary Series in Participants 18 Years and Older

Effectiveness of a booster dose of the Novavax COVID-19 Vaccine, Adjuvanted was based on assessment of neutralizing antibody titers (MN_{50}) against the original SARS-CoV-2 strain (SARS-CoV-2 hCoV-19/Australia/VIC01/2020). Immunogenicity analyses compared the MN_{50} titers following the booster dose to the MN_{50} titers following the primary series.

In the open-label booster phase of Study 1, participants 18 years of age and older received a single booster dose of the Novavax COVID-19 Vaccine, Adjuvanted at least 6 months after completion of the primary series. A subset of 243 participants were included in the per-protocol immunogenicity (PP-IMM) analysis set, did not have serologic or virologic evidence (if available) of SARS-CoV-2 infection up to 28 days post booster dose. Among participants assessed for immunogenicity, 87.2% were 18-64 years of age, 12.8 % were 65 years of age and older, 51.0% were males, 49.0% were female; 15.6% were Hispanic or Latino; 81.5% were

White, 11.1% were Black or African American, 0.4% were American Indian or Alaska Native, 4.9% were Asian, and 1.6% were multiracial. The median age of participants was 52 years (range 19-79 years).

Prespecified immunogenicity non-inferiority analyses included an assessment of MN_{50} geometric mean titer (GMT) ratio and difference in seroconversion rates. Seroconversion for a participant was defined as achieving a 4-fold rise in MN_{50} from baseline (before the booster dose and before the first dose of the primary series).

The analysis of the GMT ratio of MN_{50} following the booster dose compared to the primary series met the non-inferiority criteria for a booster response (lower limit of the 95% CI > 0.67) and point estimate > 0.83.

The lower limit of the two-sided 95% CI for the difference in seroconversion rates was -14.4%, which did not meet the non-inferiority criteria for a booster response (lower limit of 95% CI for the percentage difference of ≥ -10%). These analyses are summarized in Table 8 and Table 9.

Table 8 Neutralizing Antibody Geometric Titers (MN_{50}) Against the Original SARS-CoV-2 Virus Strain (SARS CoV-2 hCoV-19/Australia/VIC01/2020) at 28 Days after a Booster Dose Versus 14 Days After Completion of the Primary Series, Participants ≥ 18 Years of Age, PP-IMM Analysis Set[1]

Booster Dose (N = 239)[2] GMT (95% CI)[3]	Primary Series (N = 239) GMT (95% CI)[3]	GMT Ratio (Booster/Primary Series) (95% CI)[1]	Met Success Criteria
5075.6 (4448.3, 5791.4)	1505.7 (1244.1, 1822.3)	3.4 (2.8, 4.0)	Lower limit of 95% CI > 0.67 and point estimate > 0.83 criteria: Yes

Abbreviations: CI = confidence interval; GMT = geometric mean titer; MN_{50} = microneutralization assay with an inhibitory concentration of 50%; PP-IMM = Per-Protocol Immunogenicity.

[1] PP-IMM Analysis Set included participants who received two doses (0.5 mL 3 weeks apart) of the Novavax COVID-19 Vaccine, Adjuvanted in the initial vaccination period or in the blinded crossover vaccination period, had an immunogenicity blood sample collected at Day 35, did not have serologic or virologic evidence (if available) of SARS-CoV-2 infection up to 28 days post booster dose, did not receive an emergency use authorized COVID-19 vaccine, received the booster dose, and remained blinded on study and without major protocol deviations until 7 days post-crossover Dose.

[2] The analysis included a total of 239 participants of the PP-IMM analysis set who had immunogenicity data available for both the booster and primary series.

[3] The 95% CI for GMT and GMT ratio were calculated based on the t-distribution of the log-transformed values, then back transformed to the original scale for presentation.

Note: The median duration between the time of the second dose of the Novavax COVID-19 Vaccine, Adjuvanted and the time of the booster dose was 10 months.

Table 9 Seroconversion Rates Against the Original SARS-CoV-2 Strain (SARS-CoV-2 hCoV-19/Australia/VIC01/2020) at 28 Days after a Booster Dose Versus 14 Days After Completion of the Primary Series, Participants ≥ 18 Years of Age, PP-IMM Analysis Set[1]

Booster Dose (N = 239)[2] SCR n (%) (95% CI)[3]	Primary Series (N = 239) SCR n (%) (95% CI)[3]	Difference in SCR[4] (Booster-Primary Series) (95% CI)[5]	Met Success Criteria[6]
204 (85.4) (80.2, 89.6)	226 (94.6) (90.9, 97.1)	-9.2% (-14.4%, -4.5 %)	Lower limit of 95% CI > -10% criterion: No

Abbreviations: CI = confidence interval; PP-IMM = Per-Protocol Immunogenicity; SCR = seroconversion rate.

[1] PP-IMM Analysis Set included participants who received two doses (0.5 mL 3 weeks apart) of the Novavax COVID-19 Vaccine, Adjuvanted in the initial vaccination period or in the blinded crossover vaccination period, had an immunogenicity blood sample collected at Day 35, did not have serologic or virologic evidence (if available) of SARS-CoV-2 infection up to 28 days post booster dose, did not receive an emergency use authorized COVID-19 vaccine, received the booster dose, and remained blinded on study and without major protocol deviations until 7 days post-crossover Dose 2.

[2] The analysis included a total of 239 participants of the PP-IMM analysis set who had immunogenicity data (microneutralization) available for both the booster and primary series

[3] 95% CI is based on the Clopper-Pearson method.

[4] Based on the Tango method.

[5] Comparison between SCR of 28 days post-booster relative to time of booster and SCR of 14 days after second dose of the primary series relative to time of first dose.

[6] Non-inferiority of the single booster dose was achieved if the lower limit of the 95% CI for the difference of the proportion of participants with SCR at 28 days after a single booster dose relative to the time of booster vaccination versus at 14 days after the second dose of the Novavax COVID-19 Vaccine, Adjuvanted relative to the time of first vaccination was > -10%.

Note: SCR was defined as the proportion of participants with post-vaccination levels ≥ 4-fold higher than the baseline levels.

Note: The median duration between the time of the second dose of the Novavax COVID-19 Vaccine, Adjuvanted and the time of the booster dose was 10 months.

An additional descriptive analysis evaluated seroconversion rates using baseline neutralizing antibody titers prior to Dose 1 of the primary series. As shown in Table 10, the booster dose seroconversion rate, with seroconversion defined as at least a 4-fold rise relative to the time of first dose, was 98.3%. The difference in seroconversion rates in this post-hoc analysis was 3.8% (95% CI: 2.0%, 7.0%).

Table 10 Analysis of Seroconversion Rates Against the Original SARS-CoV-2 Strain (SARS CoV-2 hCoV-19/Australia/VIC01/2020) at 28 Days after a Booster Dose Versus 14 Days After Completion of the Primary Series, Participants ≥ 18 Years of Age, PP-IMM Analysis Set[1]

Booster Dose (N = 239)[2] SCR n (%) (95% CI)[3]	Primary Series (N = 239) SCR n (%) (95% CI)[3]	Difference in SCR[4] (Booster-Primary Series) (95% CI)[5]
235 (98.3) (95.8, 99.5)	226 (94.6) (90.9, 97.1)	3.8% (2.0%, 7.0%)

Abbreviations: CI = confidence interval; PP-IMM = Per-Protocol Immunogenicity; SCR = seroconversion rate.

[1] PP-IMM Analysis Set included all participants who received two doses (0.5 mL 3 weeks apart) of the Novavax COVID-19 Vaccine, Adjuvanted in the initial vaccination period or in the blinded crossover vaccination period, had an immunogenicity blood sample collected at Day 35, did not have serologic or virologic evidence (if available) of SARS-CoV-2 infection up to 28 days post booster dose, did not receive an emergency use authorized COVID-19 vaccine, received the booster dose, and remained blinded on study and without major protocol deviations until 7 days post-crossover Dose 2.

[2] The analysis included a total of 239 participants of the PP-IMM analysis set who had immunogenicity data (microneutralization) available for both the booster and primary series

[3] 95% CI is based on the Clopper-Pearson method.

[4] Based on the Tango method.

[5] Comparison between SCR of 28 days post-booster relative to time of first dose and SCR of 14 days after second dose of the primary series relative to time of first dose.

Note: SCR was defined as the proportion of participants with post-vaccination levels ≥ 4-fold higher than at the time of the first dose.

Note: The median duration between the time of the second dose of the Novavax COVID-19 Vaccine, Adjuvanted and the time of the booster dose was 10 months.

18.4 Immunogenicity of a Booster Dose Following Primary Vaccination with Another Authorized or Approved COVID-19 Vaccine

Effectiveness of a Novavax COVID-19 Vaccine, Adjuvanted booster dose in individuals who completed primary vaccination with another authorized or approved COVID-19 vaccine is inferred from immunogenicity data reported from an independent study conducted in the United Kingdom (ISRCTN 73765130). This multicenter, randomized, controlled Phase 2 trial investigated the immunogenicity of a single booster dose of Novavax COVID-19 Vaccine, Adjuvanted in participants who had received two doses of the Pfizer-BioNTech COVID-19 Vaccine as a primary vaccination series. Participants included adults aged 30 years and older with no history of laboratory-confirmed SARS-CoV-2 infection. The Novavax COVID-19 Vaccine, Adjuvanted was administered at least 84 days after completion of a Pfizer-BioNTech COVID-19 Vaccine primary series in 114 participants. Neutralizing antibody titers measured by a microneutralization assay were assessed prior to the booster dose and 28 days post-booster dose. A booster response to the Novavax COVID-19 Vaccine, Adjuvanted was demonstrated.

19 HOW SUPPLIED/STORAGE AND HANDLING

The Novavax COVID-19 Vaccine, Adjuvanted is supplied in:

- Carton (NDC 80631-100-10) containing 10 multi-dose vials (NDC 80631-100-01). Each multi-dose vial contains 10 doses of 0.5 mL each.

- Carton (NDC 80631-102-10) containing 10 multi-dose vials (NDC 80631-102-01). Each multidose vial contains 5 doses of 0.5 mL each.

Storage of Unpunctured Vial

Store the unpunctured multi-dose vaccine vial in a refrigerator between 2 to 8°C (36 to 46°F).

Do not freeze.

Protect from light.

Storage After First Needle Puncture of the Vial

After first puncture, hold the vial between 2 to 25°C (36 to 77°F) for up to 6 hours. Discard the vial 6 hours after the first puncture.

20 PATIENT COUNSELING INFORMATION

Advise the recipient or caregiver to read the Fact Sheet for Recipients and Caregivers.

The vaccination provider must include vaccination information in the state/local jurisdiction's Immunization Information System (IIS) or other designated system. Advise recipient or caregiver that more information about IISs can be found at: https://www.cdc.gov/vaccines/programs/iis/about.html.

21 CONTACT INFORMATION

For general questions, visit the website or call the telephone number provided below.

Website	Telephone number
www.NovavaxCovidVaccine.com	1-844-NOVAVAX (1-844-668-2829)

This Full EUA Prescribing Information may have been updated. For the most recent Full EUA Prescribing Information, please see www.NovavaxCovidVaccine.com.

Manufactured for:
Novavax, Inc., Gaithersburg, MD, 20878

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