News Release

**FOR IMMEDIATE RELEASE**

# U.S. FDA Approves Merck's VAXNEUVANCE™ (Pneumococcal 15-valent Conjugate Vaccine) for the Prevention of Invasive Pneumococcal Disease in Infants and Children

## Clinical data supporting approval demonstrated non-inferior immune responses for all serotypes shared with PCV13 following a four-dose series and superior immune responses for important disease-causing shared serotype 3 and unique serotypes 22F and 33F compared to PCV13

## With this expanded indication, VAXNEUVANCE is the first pneumococcal conjugate vaccine approved in almost a decade to help protect pediatric populations against invasive pneumococcal disease

RAHWAY, N.J.–(BUSINESS WIRE)– Merck (NYSE: MRK), known as MSD outside the United States and Canada, announced today that the U.S. Food and Drug Administration (FDA) has approved an expanded indication for VAXNEUVANCE™ (Pneumococcal 15-valent Conjugate Vaccine) (pronounced VAKS-noo-vans) to include children 6 weeks through 17 years of age. VAXNEUVANCE is now indicated for active immunization for the prevention of invasive disease caused by *Streptococcus pneumoniae* serotypes 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, 22F, 23F and 33F in individuals 6 weeks of age and older. The approval follows the FDA's Priority Review of Merck's supplemental application. VAXNEUVANCE is contraindicated for individuals with a severe allergic reaction (e.g., anaphylaxis) to any component of VAXNEUVANCE or to diphtheria toxoid; see additional Select Safety Information below.

The U.S. Centers for Disease Control and Prevention's (CDC) Advisory Committee on Immunization Practices (ACIP) is expected to meet today to discuss and make recommendations on the use of VAXNEUVANCE in pediatric populations.

"Despite decreases in incidence of invasive pneumococcal disease in children, certain key serotypes continue to cause serious illness that can lead to death in children under the age of 5, with serotypes 3, 22F and 33F responsible for more than a quarter of all invasive pneumococcal disease cases in this population," said Dr. Steven Shapiro, chairman, department of pediatrics, Jefferson Abington Hospital, and investigator for the PNEU-PED trial. "With the robust clinical data supporting VAXNEUVANCE and this FDA approval, VAXNEUVANCE will be an important new option to help advance protection for children."

Invasive pneumococcal disease (IPD) is an infection caused by the bacterium *Streptococcus pneumoniae*, or pneumococcus. While there are approximately 100 different types of *S. pneumoniae*, called serotypes, a smaller number of serotypes are responsible for

IPD in children. Serotypes 3, 22F and 33F are three of the top five serotypes causing childhood cases of IPD. IPD can lead to hospitalization or death. Some examples of IPD are bacteremia (an infection in the blood) and meningitis (an infection of the coverings of the brain and spinal cord), which can also result in long-term neurological complications. Children under the age of 2 are particularly vulnerable to IPD.

The FDA's approval was based on data from seven randomized, double-blind clinical studies assessing safety, tolerability and immunogenicity of VAXNEUVANCE in infants, children and adolescents (see "Clinical Data Supporting FDA Approval" below for additional details). Clinical data from the pivotal study showed that immune responses elicited by VAXNEUVANCE following a four-dose pediatric series were non-inferior to the currently available 13-valent pneumococcal conjugate vaccine (PCV13) for the 13 shared serotypes based on serotype-specific immunoglobulin G (IgG) geometric mean concentrations (GMCs).

In a secondary analysis, immune responses for VAXNEUVANCE following a four-dose pediatric series were superior to PCV13 for shared serotype 3 and the two serotypes unique to VAXNEUVANCE, 22F and 33F. Randomized controlled trials assessing the clinical efficacy of VAXNEUVANCE compared to PCV13 have not been conducted.

Data from the clinical program also support the use of VAXNEUVANCE concomitantly with other commonly administered routine pediatric vaccines, and in a variety of clinical settings, such as interchangeable use following initiation of an infant vaccination schedule with PCV13 or in a catch-up setting for older children who are either pneumococcal vaccine-naïve or who previously received an incomplete series of another PCV. Additionally, data support the use of VAXNEUVANCE in special populations, such as in preterm infants and children living with HIV infection or sickle cell disease.

"Our goal with VAXNEUVANCE is to expand coverage of key invasive disease-causing serotypes and provide a strong immune response to serotypes that pose substantial risk to infants and children," said Dr. Eliav Barr, senior vice president, head of global clinical development and chief medical officer, Merck Research Laboratories. "With this approval, we bring forward our first pediatric pneumococcal conjugate vaccine – and the first pediatric pneumococcal conjugate vaccine to be approved in almost a decade – building on our commitment to preventing invasive pneumococcal disease and on our legacy in pediatric vaccine development. We thank the investigators and the families of our clinical trial participants for participating in the research studies and the role they played in this milestone."

**About VAXNEUVANCE (Pneumococcal 15-valent Conjugate Vaccine)**

VAXNEUVANCE, Merck's 15-valent pneumococcal conjugate vaccine, consists of purified capsular polysaccharides from *S. pneumoniae* serotypes 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, 22F, 23F and 33F individually conjugated to $CRM_{197}$ carrier protein. VAXNEUVANCE is indicated for active immunization of individuals 6 weeks of age and older for the prevention of invasive disease caused by the *S. pneumoniae* serotypes contained in the vaccine. The FDA initially approved VAXNEUVANCE in July 2021. The FDA previously granted

VAXNEUVANCE Breakthrough Therapy designation and Priority Review for the pediatric indication.

**Select Safety Information for VAXNEUVANCE for infants and children**

Do not administer VAXNEUVANCE to individuals with a severe allergic reaction (e.g., anaphylaxis) to any component of VAXNEUVANCE or to diphtheria toxoid.

Some individuals with altered immunocompetence, including those receiving immunosuppressive therapy, may have a reduced immune response to VAXNEUVANCE.

Apnea following intramuscular vaccination has been observed in some infants born prematurely. Vaccination of premature infants should be based on the infant's medical status and the potential benefits and possible risks.

The most commonly reported solicited adverse reactions in children vaccinated with a four-dose series at 2, 4, 6, and 12 through 15 months of age, provided as a range across the series, were: irritability (57.3% to 63.4%), somnolence (24.2% to 47.5%), injection-site pain (25.9% to 40.3%), fever ≥38.0°C (13.3% to 20.4%), decreased appetite (14.1% to 19.0%), injection-site induration (13.2% to 15.4%), injection-site erythema (13.7% to 21.4%) and injection-site swelling (11.3% to 13.4%).

The most commonly reported solicited adverse reactions in children and adolescents 2 through 17 years of age vaccinated with a single dose were: injection-site pain (54.8%), myalgia (23.7%), injection-site swelling (20.9%), injection-site erythema (19.2%), fatigue (15.8%), headache (11.9%) and injection-site induration (6.8%).

Vaccination with VAXNEUVANCE may not protect all vaccine recipients.

**Dosage and administration for VAXNEUVANCE for infants and children**

VAXNEUVANCE is for intramuscular injection only and each dose is 0.5 mL. Administer VAXNEUVANCE as a four-dose series at 2, 4, 6, and 12 through 15 months of age. Administer VAXNEUVANCE as a single dose in children and adolescents 2 through 17 years of age who have received an incomplete series of another pneumococcal conjugate vaccine.

**Clinical data supporting FDA approval of VAXNEUVANCE in children 6 weeks through 17 years of age**

VAXNEUVANCE was approved for use in infants and children based on data from seven randomized, double-blind clinical studies designed to evaluate its safety, tolerability and immunogenicity. These clinical studies included:

- **Children receiving a four-dose series.** The pivotal Phase 3, multicenter, randomized, double-blind, active comparator-controlled study evaluated the safety, tolerability and immunogenicity of a four-dose series of VAXNEUVANCE in healthy infants (n=1720) (V114-029/PNEU-PED [NCT03893448]). In the study, participants

were randomized one-to-one to receive a four-dose series of VAXNEUVANCE or PCV13 at 2, 4, 6, and 12-15 months of age.

The assessed immune responses included serotype specific IgG response rates against capsular polysaccharides of *S. pneumoniae* at 30 days post-dose 3 (PD3) and IgG geometric mean concentrations (GMCs) at 30 days PD3 and post-dose 4 (PD4). Additionally, antibody responses to other routine licensed pediatric vaccines were evaluated when administered concomitantly with VAXNEUVANCE or PCV13.

VAXNEUVANCE elicited immune responses for all 15 serotypes contained in the vaccine. Based on serotype-specific IgG GMCs, at 30 days PD4, VAXNEUVANCE was non-inferior to PCV13 for all 13 shared serotypes and the two serotypes unique to VAXNEUVANCE, 22F and 33F. Serotypes 22F and 33F were compared with serotype 4, which had the lowest IgG GMC of all shared serotypes in PCV13, excluding serotype 3. Results of the secondary analysis showed superior immune responses for VAXNEUVANCE in comparison to PCV13 for serotypes 3, 22F and 33F.

- **PCV interchangeability.** A Phase 3, randomized, double-blind, active comparator-controlled, descriptive study evaluated the interchangeability of VAXNEUVANCE and PCV13 with respect to safety, tolerability and immunogenicity in healthy infants (n=900) (V114-027/PNEU-DIRECTION [NCT03620162]). The study demonstrated generally comparable immune responses for participants completing the vaccination series with VAXNEUVANCE compared to those who completed series with PCV13, for the 13 shared serotypes. The safety profile observed when VAXNEUVANCE was used to complete a four-dose pneumococcal conjugate vaccine series initiated with PCV13 was similar to the safety profile following a complete four-dose regimen of either VAXNEUVANCE or PCV13.

- **Use as part of a catch-up series.** A Phase 3, randomized, double-blind, active comparator-controlled, descriptive study evaluated the safety, tolerability and immunogenicity of catch-up vaccination regimens of VAXNEUVANCE in healthy infants, children and adolescents 7 months to 17 years of age (n=606) (V114-024/PNEU-PLAN [NCT03885934]). The study demonstrated generally comparable immune responses after receipt of the last dose for the 13 serotypes targeted by VAXNEUVANCE and PCV13, and higher immune responses for the two serotypes unique to VAXNEUVANCE, 22F and 33F.

**About Merck**

At Merck, known as MSD outside of the United States and Canada, we are unified around our purpose: We use the power of leading-edge science to save and improve lives around the world. For more than 130 years, we have brought hope to humanity through the development of important medicines and vaccines. We aspire to be the premier research-intensive biopharmaceutical company in the world – and today, we are at the forefront of

research to deliver innovative health solutions that advance the prevention and treatment of diseases in people and animals. We foster a diverse and inclusive global workforce and operate responsibly every day to enable a safe, sustainable and healthy future for all people and communities. For more information, visit www.merck.com and connect with us on Twitter, Facebook, Instagram, YouTube and LinkedIn.

**Forward-Looking Statement of Merck & Co., Inc., Rahway, N.J., USA**

This news release of Merck & Co., Inc., Rahway, N.J., USA (the "company") includes "forward-looking statements" within the meaning of the safe harbor provisions of the U.S. Private Securities Litigation Reform Act of 1995. These statements are based upon the current beliefs and expectations of the company's management and are subject to significant risks and uncertainties. There can be no guarantees with respect to pipeline candidates that the candidates will receive the necessary regulatory approvals or that they will prove to be commercially successful. If underlying assumptions prove inaccurate or risks or uncertainties materialize, actual results may differ materially from those set forth in the forward-looking statements.

Risks and uncertainties include but are not limited to, general industry conditions and competition; general economic factors, including interest rate and currency exchange rate fluctuations; the impact of the global outbreak of novel coronavirus disease (COVID-19); the impact of pharmaceutical industry regulation and health care legislation in the United States and internationally; global trends toward health care cost containment; technological advances, new products and patents attained by competitors; challenges inherent in new product development, including obtaining regulatory approval; the company's ability to accurately predict future market conditions; manufacturing difficulties or delays; financial instability of international economies and sovereign risk; dependence on the effectiveness of the company's patents and other protections for innovative products; and the exposure to litigation, including patent litigation, and/or regulatory actions.

The company undertakes no obligation to publicly update any forward-looking statement, whether as a result of new information, future events or otherwise. Additional factors that could cause results to differ materially from those described in the forward-looking statements can be found in the company's Annual Report on Form 10-K for the year ended December 31, 2021 and the company's other filings with the Securities and Exchange Commission (SEC) available at the SEC's Internet site (www.sec.gov).

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**Please see Prescribing Information for VAXNEUVANCE (Pneumococcal 15-valent Conjugate Vaccine) at https://www.merck.com/product/usa/pi_circulars/v/vaxneuvance/vaxneuvance_pi.pdf and Patient Information/Medication Guide for VAXNEUVANCE at https://www.merck.com/product/usa/pi_circulars/v/vaxneuvance/vaxneuvance_ppi.pdf.**


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| Media Contacts: | Julie Cunningham<br>(617) 519-6264 | Investor Contacts: | Peter Dannenbaum<br>(908) 740-1037 |

Kimberly Petrillo
(267) 742-2813

Alexis Constantine
(908) 740-1051