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Data From Pfizer's Adult and Pediatric Clinical Trial Programs for 20-Valent Pneumococcal Conjugate Vaccine Presented at IDWeek 2020

Wednesday, October 21, 2020 - 08:30am

- **Investigational vaccine demonstrated positive safety results and immune responses to 20 *S. pneumoniae* serotypes in adults and infants**
- **Pfizer has submitted to the FDA its biologics license application for adults 18 years of age or older and awaits acceptance for review**

NEW YORK--(BUSINESS WIRE)-- Pfizer Inc. (NYSE:PFE) today announced the full analysis from one of its Phase 3 studies (NCT03760146), which evaluated the safety and immunogenicity of its 20-valent pneumococcal conjugate vaccine (20vPnC) candidate in adults 18 years of age or older not previously vaccinated against pneumococcal disease.[1] The data from this pivotal trial were presented as part of IDWeek's virtual 2020 medical congress, along with data from a Phase 2 proof-of-concept study in infants given a four-dose pediatric series.[2]

Earlier this month, Pfizer submitted the 20vPnC biologics license application for adults 18 years of age or older to the U.S. Food and Drug Administration, and is awaiting acceptance of the application for review. Pfizer anticipates submitting the 20vPnC marketing authorization application for adults to the European Medicines Agency in Q1 2021.

The 20vPnC Phase 3 Pivotal Adult Trial

The Phase 3 randomized, double-blind trial (NCT03760146) included 902 adults aged 18 or older with no history of pneumococcal vaccination. The study was designed to compare immune responses after receipt of 20vPnC in adults ?60 years old to responses in a control group receiving Prevnar 13 or a licensed pneumococcal polysaccharide vaccine (PPSV23).[1] The study also evaluated immune responses of 20vPnC in adults 18 to 59 years (secondary endpoints) and described the safety profile of 20vPnC in all adults ?18 years old (primary endpoint).[1] Additional information about the study can be found at www.clinicaltrials.gov under the identifier NCT03760146.

In the study, researchers found that all 20 vaccine serotypes induced robust responses across three age cohorts (? 60 years, 50-59 years, 18-49 years).[1] For the primary immunogenicity objectives in adults ages 60 years or older, the ratio of serotype-specific OPA geometric mean titers (GMTs) responses one month after vaccination were noninferior for all the serotypes in common with licensed Prevnar 13 and six of the seven additional serotypes when compared to a PPSV23. One of the new seven serotypes (serotype 8) missed the noninferiority lower bound criteria of >0.5 by a small margin (0.55 [0.49, 0.62]) but showed immune responses in other immunological parameters including fold-rises in OPA titers, proportions of subjects with ?4-fold rise in OPA titers and proportions of subjects with OPA titer ? lower limit of quantification (LLOQ) after vaccination.[1]

Immune responses to 20vPnC in the younger age cohorts (18-49 years and 50-59 years) were noninferior to 20vPnC responses in adults 60-64 years; these were secondary immunogenicity endpoints.[1]

For the primary safety analysis, the frequency of adverse events among participants within 1 month after receiving 20vPnC was generally similar to participants receiving 13vPnC, including:[1]

- ?60 years: 9.8% (20vPnC) and 11.1% (13vPnC)
- 50-59 years: 10.2% (20vPnC) and 8.1% (13vPnC)
- 18-49 years: 15.2% (20vPnC) and 11.6% (13vPnC)

Vaccine related adverse events (AEs) for 20vPnC and 13vPnC respectively were (?60 years: 0.9% and 1.5%; 50-59 years: 0.9% and 0.9%; 18-49 years: 1.5% and 1.8%).[1] No serious AEs were considered vaccine related.[1] Injection site pain was the most frequently reported local reaction and most local reactions were mild or moderate in severity.[1]

Pfizer had previously announced top-line data from this Phase 3 study (NCT03760146) in March 2020.

The 20vPnC Phase 2 Infant Trial

The Phase 2 study (NCT03512288) was a multicenter, randomized, active-controlled, double-blind study with a two-arm parallel design, conducted at investigator sites in the United States. There were 460 infants ages 42 to 98 days randomized (1:1) to receive either 20vPnC or Prevnar 13 at 2, 4, and 6 months of age (infant series, Doses 1 through 3) and 12 months of age (Dose 4).[2] Other routine pediatric vaccines could be administered according to the current ACIP recommended schedule. Safety and immune responses were assessed in the study.[2]

Overall, the safety profile of a four-dose schedule of 20vPnC was consistent with 13vPnC given in the same schedule.[2] A similar percentage of infants receiving either vaccine experienced local reactions (pain at the injection site, redness, and swelling), fever, and other systemic events (decreased appetite, drowsiness, and irritability).[2]

In the study, a similar percentage of infants receiving either 20vPnC or 13vPnC experienced an adverse event (AE) within one month after Dose 3 (59% and 56%, respectively) and from Dose 4 to one month after Dose 4 (19% and 25%, respectively).[2] A total of 12 infants (5.2%) in the 20vPnC group and 5 (2.2%) in the 13vPnC group experienced a serious adverse event, none of which were considered related to the vaccine.[2]

In the descriptive immunogenicity analysis, the following results were observed:

- 20vPnC elicited pneumococcal immune responses to all 20 serotypes one month after Dose 3 as measured by both the percentages of participants with prespecified serotype-specific IgG concentrations and IgG Geometric Means Concentrations (GMCs).[2]
- Booster responses were observed for all serotypes after Dose 4 when comparing the serotype-specific IgG GMCs from one month after Dose 4 to responses both 1 month after Dose 3 and before Dose 4 indicating the induction of immunological memory.[2]
- 20vPnC elicited functional antibody responses to all 20 serotypes at one month after Dose 3 and one month after Dose 4 as measured by OPA GMTs. Boosting of OPA responses was also observed for all serotypes after Dose 4 consistent with the trend observed with IgG responses.[2]

About the 20vPnC Clinical Trial Program

“We are encouraged by the Phase 3 adult and Phase 2 pediatric data. The data suggest that 20vPnC would be anticipated to help protect against the serotypes covered by Prevnar 13, and also expand coverage to include seven additional pneumococcal serotypes causing potentially serious and life-threatening disease,” said Kathrin U. Jansen, Ph.D., Senior Vice President and Head of Vaccine Research & Development, Pfizer. “Since the 20 *S. pneumoniae* serotypes included in 20vPnC are responsible for the majority of global pneumococcal disease cases,[3,4,5,6,7,8,9] we are excited by the potential broader coverage this investigational vaccine may offer people.”

Phase 3 Adult Program

Pfizer’s Phase 3 adult clinical program for 20vPnC includes three studies, which, combined, have enrolled more than 6,000 adult subjects, including populations of vaccine-naïve adults and adults with prior pneumococcal vaccination.

Along with the study reported in this news release (NCT03760146), the other two studies include:

- **NCT03828617**: Phase 3 randomized, double-blind trial, designed to provide additional safety data and evaluate three different lots of 20vPnC in adults 18 through 49 years of age with no history of pneumococcal vaccination. More on the study can be found on www.clinicaltrials.gov under the identifier NCT03828617. Pfizer previously announced positive findings from this study in May 2020.

- **NCT03835975**: Phase 3 randomized, open-label trial, designed to describe the safety and immune response of 20vPnC in an estimated 875 adults aged 65 years or older with prior pneumococcal vaccination. More on the study can be found on www.clinicaltrials.gov under the identifier NCT03835975.

In addition, a study to assess 20vPnC given with influenza vaccine was initiated in September 2020:

- **NCT04526574**: Phase 3 randomized, double-blind trial to evaluate the safety and immunogenicity of 20vPnC when co-administered with a seasonal inactivated influenza in adults ?65 years of age. More on the study can be found on www.clinicaltrials.gov under the identifier NCT04526574.

Phase 3 Pediatric Program

In 2020, Pfizer initiated the Phase 3 clinical trial program for the pediatric indication for 20vPnC. Currently, three Phase 3 infant studies have been started; these studies will help expand the data on the safety, tolerability, and immunogenicity of 20vPnC demonstrated in the Phase 2 proof-of-concept study. These studies, collectively, are enrolling approximately 4,700 infants. These include the following:

- **NCT04382326:** A Phase 3 study that will describe the tolerability and safety, and compare immunogenicity of the 20vPnC to the 13vPnC in infants vaccinated at 2, 4, 6, and 12-15 months of age in the US. More on the study can be found on www.clinicaltrials.govunder the identifier NCT04382326.

- **NCT04379713:** A Phase 3 study that will describe tolerability and safety of 20vPnC with 13vPnC serving as the control in infants vaccinated at 2, 4, 6, and 12-15 months of age currently recruiting in North America, and Europe. More on the study can be found on www.clinicaltrials.govunder the identifier NCT04379713.

- **NCT04546425:** A Phase 3 study that will describe tolerability and safety, and compare immunogenicity of 20vPnC to 13vPnC in infants vaccinated at 2, 4, and 11-12 months of age is currently enrolling in Europe.

More on the study can be found on www.clinicaltrials.govunder the identifier NCT04546425.

About 20vPnC

Pfizer's 20vPnC vaccine candidate includes 13 serotypes already included in Prevnar 13® (pneumococcal 13-valent Conjugate Vaccine [Diphtheria CRM197 Protein]), along with seven new serotypes that are global causes of invasive pneumococcal disease (IPD),[10,11,12,13,14] and are associated with high case-fatality rates,[15,16,17,18] antibiotic resistance,[14,19,20] and/or meningitis.[21,22]

On September 20, 2018, Pfizer announced the U.S. Food and Drug Administration (FDA) granted Breakthrough Therapy Designation for 20vPnC for the prevention of invasive disease and pneumonia in adults age 18 years or older. On September 15, 2020, Pfizer's 20vPnC also received the FDA's Breakthrough Therapy Designation for the prevention of disease caused by *S. pneumoniae* serotypes in the vaccine in infants, children, and adolescents.

Breakthrough Therapy Designation is designed to expedite the development and review of drugs and vaccines that are intended to treat or prevent serious conditions and preliminary clinical evidence indicates that the drug or vaccine may demonstrate substantial improvement over available therapy on a clinically significant endpoint(s).[23] Drugs and vaccines that receive Breakthrough Therapy Designation are eligible for all features of the FDA's Fast Track designation, which may include more frequent communication with the FDA about the drug's development plan and eligibility for Accelerated Approval and Priority Review, if relevant criteria are met.[24]

The FDA previously granted Fast Track designation for 20vPnC in May 2017 for the pediatric indication[25] and in September 2017 for use in adults aged 18 years or older.[26] The FDA's Fast Track approach is a process designed to facilitate the development and expedite the review of new drugs and vaccines intended to treat or prevent serious conditions and address an unmet medical need.[24]

If approved and licensed by FDA, Pfizer's 20vPnC vaccine candidate would cover the 13 *S. pneumoniae* serotypes already in Prevnar 13® (Pneumococcal 13-valent Conjugate Vaccine [Diphtheria CRM197 Protein]) – 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F – plus seven additional serotypes (8, 10A, 11A, 12F, 15B, 22F, and 33F).

INDICATIONS FOR PREVNAR 13®

- Prevnar 13® is a vaccine approved for adults 18 years and older for the prevention of pneumococcal pneumonia and invasive disease caused by *S. pneumoniae* serotypes 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F
- Prevnar 13® is also approved for children 6 weeks through 17 years of age (prior to the 18th birthday) for the prevention of invasive disease caused by the 13 strains of *Streptococcus pneumoniae* in the vaccine, and for children 6 weeks through 5 years (prior to the 6th birthday) for the prevention of ear infections caused by 7 of the 13 strains in the vaccine
- Prevnar 13® is not 100% effective and will only help protect against the 13 strains in the vaccine

IMPORTANT SAFETY INFORMATION

- Prevnar 13® should not be given to anyone with a history of severe allergic reaction to any component of Prevnar 13® or any diphtheria toxoid–containing vaccine
- Children and adults with weakened immune systems (eg, HIV infection, leukemia) may have a reduced immune response

- In adults, the most common side effects were pain, redness, and swelling at the injection site, limitation of arm movement, fatigue, headache, muscle pain, joint pain, decreased appetite, vomiting, fever, chills, and rash
- A temporary pause of breathing following vaccination has been observed in some infants born prematurely
- The most commonly reported serious adverse events in infants and toddlers were bronchiolitis (an infection of the lungs) (0.9%), gastroenteritis (inflammation of the stomach and small intestine) (0.9%), and pneumonia (0.9%)
- In children 6 weeks through 17 years, the most common side effects were tenderness, redness, or swelling at the injection site, irritability, decreased appetite, decreased or increased sleep, and fever
- Ask your healthcare provider about the risks and benefits of Prevnar 13®. Only a healthcare provider can decide if Prevnar 13® is right for you or your child

Pfizer Inc: Breakthroughs that change patients' lives

At Pfizer, we apply science and our global resources to bring therapies to people that extend and significantly improve their lives. We strive to set the standard for quality, safety and value in the discovery, development and manufacture of health care products, including innovative medicines and vaccines. Every day, Pfizer colleagues work across developed and emerging markets to advance wellness, prevention, treatments and cures that challenge the most feared diseases of our time. Consistent with our responsibility as one of the world's premier innovative biopharmaceutical companies, we collaborate with health care providers, governments and local communities to support and expand access to reliable, affordable health care around the world. For more than 150 years, we have worked to make a difference for all who rely on us. We routinely post information that may be important to investors on our website at www.pfizer.com. In addition, to learn more, please visit us on www.pfizer.com and follow us on Twitter at @Pfizer and @Pfizer_News, LinkedIn, YouTube, and like us on Facebook at Facebook.com/Pfizer.

DISCLOSURE NOTICE:

The information contained in this release is as of October 21, 2020. Pfizer assumes no obligation to update forward?looking statements contained in this release as the result of new information or future events or developments.

This release contains forward?looking information about Pfizer's 20-Valent Pneumococcal Conjugate Vaccine (20vPnC) candidate, including expected licensure criteria and its potential benefits, that involves substantial risks and uncertainties that could cause actual results to differ materially from those expressed or implied by such statements. Risks and uncertainties include, among other things, the uncertainties inherent in research and development, including the ability to meet anticipated clinical endpoints, commencement and/or completion dates for our clinical trials, regulatory submission dates, regulatory approval dates and/or launch dates, as well as the possibility of unfavorable new clinical data and further analyses of existing clinical data; the risk that clinical trial data are subject to differing interpretations and assessments by regulatory authorities; whether regulatory authorities will be satisfied with the design of and results from our clinical studies; whether and when any biologics license applications may be filed in any additional jurisdictions for 20vPnC for adults 18 years of age or older or in any jurisdictions for 20vPnC for any indications; whether and when regulatory authorities in any jurisdictions where any applications are pending or may be submitted for 20vPnC may approve any such applications, which will depend on myriad factors, including making a determination as to whether the product's benefits outweigh its known risks and determination of the product's efficacy and, if approved, whether 20vPnC will be commercially successful; decisions by regulatory authorities impacting labeling, manufacturing processes, safety and/or other matters that could affect the availability or commercial potential of 20vPnC; uncertainties regarding the ability to obtain recommendations from vaccine technical committees

and other public health authorities regarding 20vPnC and uncertainties regarding the commercial impact of any such recommendations; the impact of COVID-19 on our business, operations and financial results; and competitive developments.

A further description of risks and uncertainties can be found in Pfizer's Annual Report on Form 10-K for the fiscal year ended December 31, 2019 and in its subsequent reports on Form 10-Q, including in the sections thereof captioned "Risk Factors" and "Forward-Looking Information and Factors That May Affect Future Results", as well as in its subsequent reports on Form 8-K, all of which are filed with the U.S. Securities and Exchange Commission and available at www.sec.gov and www.pfizer.com.

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[25] Data on file. Pfizer Inc., New York, NY
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Pfizer Media:
Jerica Pitts
(586) 883-0142
jerica.pitts@pfizer.com

Pfizer Investor:
Bryan Dunn
(212) 733-8917
bryan.dunn@pfizer.com

Source: Pfizer Inc.