Vivaldi Biosciences' Phase 2 Influenza Vaccine Shows Broad Cross-Protection and Superiority in Nonclinical Study

FORT COLLINS, Colorado – February 12, 2018 – Vivaldi Biosciences, based at the Research Innovation Center at Colorado State University and Vienna, Austria, today announced that its DeltaFLU influenza vaccine shows broad cross-protection against distantly related influenza strains, and superior protection versus a leading licensed vaccine in a recently completed nonclinical study. Vivaldi scientists took an ambitious approach in evaluating the performance of DeltaFLU against mismatched strains, by testing protective efficacy against influenza A and B strains with significant antigenic differences from the strains comprising the DeltaFLU vaccine. DeltaFLU was shown to be protective against these widely divergent strains, while the licensed vaccine showed a lack of protection.

DeltaFLU already has been evaluated in Phase 1 and 2 clinical studies involving 245 adult volunteers, showing it is safe and immunogenic. Importantly, study volunteers immunized with DeltaFLU generated antibodies in the serum and nasal mucosa that are broadly cross-reactive against mismatched strains. These clinical and nonclinical data demonstrating protective mechanisms against a broad range of influenza A and B strains are strong indicators of the potential of DeltaFLU as a universal seasonal influenza vaccine.

Licensed influenza vaccines generally rely on a good antigenic match between the vaccine strains and circulating strains for protective efficacy. Mismatches between vaccine and circulating strains frequently occur, reducing vaccine effectiveness. Influenza vaccine effectiveness typically is only 40-60%, and in some years is far lower.

In Vivaldi's nonclinical study, ferrets were immunized with a trivalent DeltaFLU vaccine, quadrivalent licensed vaccine, or placebo. The DeltaFLU vaccine and licensed vaccine contain the three or four strains, respectively, recommended by the World Health Organization for the current flu season. The ferret is the most relevant and well characterized animal model of human influenza infection and immune response. Immunized ferrets were challenged by intranasal administration of an influenza A/H1N1, A/H3N2, or B strain that circulated from 2008 until 2010. The A/H3N2 and B challenge strains are widely drifted from the A/H3N2 and B strains contained in the vaccines, with multiple antigenic changes. The A/H1N1 challenge strain is antigenically shifted from the A/H1N1 vaccine strain, containing a completely different antigen from the A/H1N1 vaccine strain.

DeltaFLU protected against all three challenge strains, as indicated by measures of symptoms and infection. For example, in assessments of fever, all ferrets immunized with DeltaFLU and subsequently challenged with one of the three divergent strains exhibited no fever or only light fever (39.5-39.9°C), with the exception of one ferret (out of 12) with moderate fever (40.1°C). In contrast, the licensed vaccine failed to protect immunized and challenged animals from fever; all 12 ferrets immunized with the licensed vaccine exhibited fever after challenge, including 5 ferrets that exhibited severe fever ($\geq$40.5°C).

Lack or reduction of shedding of challenge virus is another measurable indicator of protection against influenza infection. DeltaFLU showed superior protection versus the licensed vaccine in evaluations of shedding of the A/H1N1 and B challenge viruses. Moreover, the virus shedding data substantiated the fever data for ferrets in the A/H1N1 and B challenge groups. The A/H3N2 was a low-shedding virus in all groups; however, this challenge strain produced strong symptoms of infection in the licensed vaccine and placebo groups but not in the DeltaFLU group. Vivaldi's Chief Scientific Officer, Thomas Muster, PhD, will present data from this and additional ongoing studies on April 4, 2018 at the World Vaccine Congress in Washington, DC.

DeltaFLU is produced in a high-efficiency, high-yield Vero cell production system that can provide advantages in terms of speed, capacity, reliability, and cost versus the decades-old egg-based production process used for the vast majority of influenza vaccines. Recent studies indicate that egg-based production induces antigenic changes that may reduce vaccine efficacy.

About Vivaldi Biosciences

Vivaldi Biosciences is developing its DeltaFLU influenza vaccine to provide broad cross-protection and superior efficacy in the prophylaxis of seasonal and pandemic influenza. DeltaFLU is composed of influenza vaccine strains genetically modified by deletion of the gene for nonstructural protein 1 (NS1). This protein blocks interferon, a key component of the immune system's response to viral infection. Since DeltaFLU strains lack the ability to suppress the host interferon response, they induce high levels of interferon, achieving a natural adjuvant effect that stimulates the immune system's T cells and antibody-producing B cells. Administered as a nasal spray, DeltaFLU generates a first line of defense at the point of entry of circulating viruses. In clinical trials, DeltaFLU has been shown to induce antibodies in the nasal mucosa that cross-neutralize influenza strains of different subtypes; for example, a DeltaFLU A/H1N1 vaccine strain induces mucosal antibodies that neutralize influenza viruses of the A/H3N2 and A/H5N1 subtypes. DeltaFLU strains are replication-deficient in animals and humans and are not shed by the recipient, providing significant safety advantages. Additional information about Vivaldi can be found at http://www.vivaldibiosciences.com.

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Forward-Looking Statements

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funding on commercially reasonable terms, the regulatory environment and other risks the Company may identify from time to time in the future. These factors are not necessarily all of the important factors that could cause our actual results, performance or achievements to differ materially from those expressed in or implied by any of our forward-looking statements. These forward-looking statements speak only as of the date of this communication and we undertake no obligation to update or revise any forward-looking statement, whether as a result of new information, future events and developments or otherwise, except as required by law. If we update one or more forward-looking statements, no inference should be drawn that we will make additional updates with respect to those or other forward-looking statements. This press release should not constitute an offer to sell or a solicitation of an offer to buy securities.