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Influenza*

FLUGEN'S M2SR INFLUENZA VACCINE SUCCEEDS IN PHASE 2 HUMAN CHALLENGE TRIAL AGAINST A HIGHLY MISMATCHED VIRUS

—Topline data shows first flu vaccine to demonstrate protection against a multi-season mismatched H3N2 strain in a human challenge clinical trial—

— Intranasal administration of M2SR well-tolerated in trial —

— Protection against influenza challenge correlated with serum response to M2SR—

—Important step closer to a universal influenza vaccine—

MADISON, Wis., February 12, 2019 — FluGen, Inc. today announced preliminary data from a human challenge trial with its investigational intranasal M2SR vaccine showing, for the first time, protection against a highly mismatched influenza virus. This major step toward demonstrating breadth of protection is key to developing a universal flu vaccine against flu viruses that have significantly drifted from the strains contained in the vaccines.

The goal of FluGen's Phase 2 M2SR study was to test whether its flu vaccine could demonstrate the broad protection required during years when there is a mismatch between the vaccine and the circulating influenza strain. The topline results from a six-year mismatch confirm the strong results seen in Phase 1 immunogenicity and preclinical challenge studies.

The double-blind, placebo-controlled Phase 2 clinical trial of 99 healthy adults, sponsored by the U.S. Department of Defense, compared FluGen's M2SR vaccine matching a virus from 2007 against a challenge with a live H3N2 influenza virus from the 2014-15 flu season. Study subjects were randomized 1:1 to receive either intranasal placebo, or a single intranasal dose of M2SR vaccine. The development of M2SR has also been supported by the National Institutes for Allergy and Infectious Diseases (NIAID) division of the National Institutes of Health (NIH).

According to the Centers for Disease Control and Prevention, the effectiveness of the marketed inactivated flu vaccine from the 2014-15 flu season was just 19 percent overall and close to zero percent in those 65 and older. The mismatch tested in the FluGen clinical study was significantly greater than the mismatch between the marketed injectable vaccine and the predominant circulating influenza virus in 2014-15.

Intranasal flu vaccines historically have not generated serum responses that have correlated with vaccine effectiveness in adults. However, despite the significant mismatch in this study, more than half of the participants receiving M2SR showed a serum antibody response to the vaccine and these subjects showed a 34 percent reduction of viral load during the challenge phase of the study, compared to placebo. Subjects in the trial who developed antibody to both the vaccine and challenge virus showed a 62 percent reduction in viral load, compared to placebo.



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The same groups showed 51 percent and 56 percent reductions, respectively, in symptom scores, illustrating that the M2SR vaccine reduced both viral load and symptoms when challenged with a high dose of highly mismatched H3N2 influenza virus. The correlation between serum markers and effectiveness in the trial is expected to accelerate further development of M2SR.

The need to frequently change the strains of influenza included in the annual flu vaccine due to seasonal influenza drift and frequent antigenic mismatch is a significant problem that leads to decreased vaccine effectiveness. In the 14 influenza seasons since 2004, there have been nine H3N2 vaccine changes (drifts), and in three of these seasons the licensed inactivated vaccine was highly mismatched to the circulating virus. When the vaccine is mismatched and has low efficacy, the resulting toll includes increased hospitalizations and death from influenza.

“The problem of seasonal drift and mismatches between the annual influenza vaccine and circulating strains is a significant public health challenge and contributes to the low effectiveness and increased illness and mortality we see too often,” said Dr. Robert Belshe, chair of the FluGen clinical advisory board and the Diana and J. Joseph Adorjan Endowed Professor of Infectious Diseases and Immunology, Emeritus, at Saint Louis University.

“The remarkable results from this trial of FluGen’s M2SR vaccine mark an important step forward in the development of a more universal flu vaccine and take some of the guess work out of picking strains to put in the vaccine. No one, to my knowledge, has ever tried a study like this before,” Belshe added.

The company plans to complete its data analysis and present the data in an upcoming peer reviewed forum.

“Considering the generally low vaccine effectiveness of marketed injectable vaccines, as well as the serious consequences when the influenza virus drifts just slightly from the currently licensed annual flu vaccine, we wanted to better understand how broadly FluGen’s M2SR vaccine could protect if the flu virus had dramatically mutated not one year, but over six influenza seasons,” said Paul Radspinner, chief executive officer of FluGen.

“With the financial support we have in place from our investors and government partners, we are excited to advance the development of M2SR based on these significant results,” Radspinner added.



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About M2SR

FluGen's M2SR vaccine utilizes a proprietary M2 deleted, single replication (M2SR) influenza virus. The M2 gene is essential for the influenza virus to spread in the patient and the deletion of the M2 gene restricts the virus to a single replication cycle in the host. The body recognizes M2SR as an influenza infection and activates its robust immune response, but, because the virus can only replicate once, it cannot spread to other cells and cause symptoms of a real-world infection.

Patients naturally infected with wild type influenza often are protected from future influenza illness for many years. By convincing the body it has been infected with influenza, the M2SR vaccine is designed to activate this broad and durable wild type immune response, without causing influenza disease.

Study Details

In the ongoing study, being conducted by SGS in Belgium, subjects were randomized 1:1 to receive either intranasal placebo, or a single intranasal dose of investigational M2SR vaccine, manufactured with the A/Brisbane/10/2007, H3N2 strain of influenza, which was utilized in marketed influenza vaccines during the 2008-2010 influenza seasons.

Subjects were then challenged intranasally with the A/Belgium/4217/2015, H3N2 influenza virus, which is a genetically drifted virus that caused outbreaks of influenza in 2014-15. Following influenza challenge, subjects were assessed for safety, infection with the challenge strain and clinical signs and symptoms. Subjects are being followed on an ongoing basis for four months. While all subjects have completed vaccination and challenge, the full study is expected to be completed sometime in the second quarter of this year.

The study is supported by a \$14.4 million grant from the Department of Defense. The U.S. Army Medical Research Acquisition Activity is the awarding and administering acquisition office and this work was supported by the Office of the Assistant Secretary of Defense for Health Affairs through the Peer Reviewed Medical Research Program under Award No. W81XWH-17-1-0430.

A prior Phase 1a study of FluGen's M2SR vaccine in 96 subjects showed the vaccine to be generally safe and well tolerated, and to generate a robust immune response that was dose related.



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About FluGen, Inc.

FluGen, Inc. is a clinical stage vaccine company focused on improving the breadth and effectiveness of influenza vaccines. The company's technology comes from the laboratory of Dr. Yoshihiro Kawaoka at the University of Wisconsin, Madison. FluGen's lead product candidate, an M2SR vaccine, is a universal flu vaccine which is based on the knowledge that a natural or wild-type flu infection prevents people from being infected in subsequent years. The M2SR vaccine has demonstrated a robust immunology profile that works through multiple immune pathways systems and appears to trick the body into believing it has been infected, triggering a robust immune response while not displaying flu symptoms.

For more information about FluGen, Inc., please visit <http://www.FluGen.com/>

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