More Than Vaccines: Tonix Programs Address the Spectrum of Covid-19 Problems from Prevention, to Infection to Post-Viral Syndrome

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Benzinga• July 15, 2021

With the Covid-19 pandemic becoming more contained in certain geographic areas, medical researchers are turning their attention to a wider range of prevention and treatment tools for what many consider to be the long road ahead in managing the SARS-CoV-2 virus, its variants and the post-Covid-19 syndrome called “Long Covid”.

Most experts agree that the disease’s pandemic stage will transition into an endemic in which SARS-CoV-2 or variants will emerge and spread unpredictably in different parts of the world at different times with different degrees of severity.

Tonix Pharmaceuticals (**NASDAQ: TNXP**) is one of the few companies pursuing vaccines and therapeutics that address the spectrum of Covid-19 needs ranging from prevention to acute infection to post-viral syndromes.

Recent developments are taking the approximately $400 million market cap NASDAQ-listed biopharmaceutical company beyond its flagship vaccine Covid-19 program to include new therapeutics for acute treatment of SARS-CoV-2 infection, management of chronic Long Covid, and a diagnostic skin test to measure T cell immunity.

Benzinga recently caught up with Tonix CEO Seth Lederman, MD to learn more about the company’s expanded footprint in Covid-19 programs.

Dr. Lederman believes Tonix is well positioned to make major contributions to the challenges presented by Covid-19. “The knowledge we gained working with the SARS-CoV-2 virus for our vaccines, and our long experience in CNS disorders is enabling us to develop a broad spectrum of Covid-19 solutions,” he said.

Current Concerns

Even as hundreds of millions of people in the US have been vaccinated, lots of questions remain about the duration of protection afforded by the Emergency Use Authorization vaccines that appear to have been valuable in the early stages of the pandemic.

Because the modified mRNA vaccines utilize new and previously untested technology, there is uncertainty about the duration of immunity they provide. Emergency Use Authorization was based on efficacy data from three months after vaccination. It is not known if these vaccines provide protection one year after vaccination or how effective they may be against emerging variants.

Public health officials fear public health policy based on the current vaccines alone may become problematic if the protection they provide has limited duration. While the vaccines from **Moderna (NASDAQ: MRNA**) and **Pfizer, Inc. PFE 0.5%** are effective, they require a two-shot regimen over several weeks to about a month. The only Emergency Use Authorization that is a one shot vaccine, or 'one and done', is made by **Johnson & Johnson JNJ 0.14%**, but it has recently fallen into disfavor for the US market due to potential increased risk of rare types of thrombosis and because of manufacturing issues.

Most experts believe different vaccines may be needed down the road if the current mRNA vaccines don't provide prolonged immunity.

Acute Covid-19 treatment options are another issue. Only one antiviral drug, remdesivir, is FDA approved for treating acute Covid-19. While remdesivir represents an important advance, its activity is limited and there is still an unmet need for new Covid-19 antivirals to decrease hospitalization and the need for further interventions.

No medicine for the treatment of Long Covid has been approved. The condition is characterized by myriad symptoms, including chronic pain, poor sleep, fatigue and 'brain fog' and is believed to afflict roughly 30 percent of individuals recovering from Covid-19. Late last year, Congress allocated $1.15 billion to research Long Covid.

To top it off, there is currently a need for non-laboratory methods to tell whether someone has T cell immunity to SARS-COV-2. This is seen as an important need because it is unknown whether or to what extent the mRNA vaccines induce T cell immunity and if so, how long protection lasts after vaccination. It is also unknown how long T cell immunity lasts after recovering from Covid-19 naturally.

Tonix's expanded COVID-19 solutions portfolio aims to address a number of these unmet needs.

Positive Vaccine Results in Animals

The company recently reported positive preliminary Covid-19 vaccine efficacy results in nonhuman primates with its TNX-1800 vaccine, a modified live attenuated horsepox virus vaccine.

Tonix TNX-1800 is based on technology developed more than 200 years ago by Dr. Edward Jenner who pioneered the original vaccine against smallpox, the only viral

disease to ever be fully eradicated. TNX-1800, which uses Jenner's technology as its backbone, is engineered to express the Spike protein in SARS-CoV-2 to generate a strong T cell response and provide immunity.

The animal efficacy trial was conducted at Southern Research. It tested high and low doses for safety, protective efficacy, and immunogenicity. On the 14th day after a single vaccination, the TNX-1800 vaccinated animals, from the high and low dose groups, had-SARS-CoV-2 neutralizing antibodies. Those vaccinated with a control vaccine did not make neutralizing antibodies. At the end of 41 days after vaccination, the animals were challenged with live viruses, and the protection was assessed after 6 days. The animals administered TNX-1800 had undetectable SARS-CoV-2 in either their upper or lower airways.

All animals vaccinated with TNX-1800 manifested a 'take', which is a skin reaction to the vaccine. The 'take' is a measure of functional T-cell immunity and in other viral diseases is predictive of long-term immunity.

An important feature of T cell immunity is durability, as was shown with Jenner's smallpox vaccine, which provided protection for decades and longer. This type of durable immunity could potentially bring the same benefit to containing Covid-19 from the original Wuhan strain and from variants.

Unlike current vaccines, the company expects that TNX-1800 can be manufactured using standard bioreactor equipment and can be shipped using standard refrigeration. Because the dose is low relative to non-replicating vaccines, Tonix expects to fill 100 doses per vial, a glass sparing feature.

Tonix believes T cell immunity provides the best chances of being protected against SARS-CoV-2 variants. Tonix also believes its vaccine may provide protection against as smallpox due its use of Jenner's backbone. Such a 'bivalent' vaccine would be important in protection against the malicious reintroduction of smallpox. Many suspect that rogue nations may be encouraged by the devastation of Covid-19 to consider a 'low-tech' approach to biowarfare, particularly since the U.S. stopped vaccinating against smallpox in about 1970.

The current Emergency Use Authorization Covid-19 vaccines based on mRNA may need a booster dose, which is a concept already advanced by Pfizer. However, it is unknown if boosters will work or how logistically viable the idea is. The reason the efficacy of boosters is unknown is because the modified mRNA vaccine technology is brand new and the Covid-19 vaccines are the first products widely used with this technology. The reason the logistical viability is unknown is because a daunting amount of vaccine and glass would needed to annually revaccinate a substantial proportion of the world's population.

TNX-1800 is being developed as a single dose vaccine. A one-shot vaccine is believed to offer better compliance of immunity and could more easily facilitate a global immunization strategy compared to vaccines that require two-doses separated by a few weeks. Tonix plans to advance TNX-1800 into human testing during the first half of next year.

Acute Infection, Chronic Disease, and Testing

Tonix's antiviral SARS-CoV-2 inhibitor, TNX-3500, has been shown in early studies to significantly inhibit the viral cause of COVID-19 and to potentiate remdesivir, which is Gilead's FDA approved antiviral marketed as Veklury®.

The TNX-3500 antiviral candidate, licensed from OyaGen in April this year, has undergone extensive *in vitro* testing at the NIH which showed its potency is 65 times greater than remdesivir in a head-to-head comparison in inhibiting live SARS-CoV-2 virus. The studies also showed that combination studies of TNX-3500 and remdesivir produced greater activity against SARS-CoV-2 live virus than either agent alone.

The active ingredient in TNX-3500 has been studied for safety in humans in prior studies on cancer patients at the U.S. National Cancer Institute.

Because of the prior human safety tests and the agent's significant performance in tissue culture, Tonix believes TNX-3500 may qualify for expediated clinical development.

Tonix believes it can also move quickly with its program (TNX-102 SL) for Long Covid due to its long experience in fibromyalgia –a condition whose symptoms overlap those observed in Long Covid patients.

Tonix said it plans to meet with the FDA in the third quarter of this year to seek agreement on protocols for a potentially pivotal Phase 2 trial in Long Covid with TNX-102 SL, the same agent it is developing for fibromyalgia in a Phase 3 program.

The second of two Phase 3 trails in fibromyalgia is nearing completion with an interim analysis due in this quarter (3rd quarter 2021). Positive results were reported in the first Phase 3 trial in fibromyalgia with a *p*-value of 0.01.

Earlier, this year, Tonix announced plans to develop a skin test to measure T cell immunity to the SARS-CoV-2 virus. The company believes this could make a significant contribution for monitoring public health and to evaluate long term immunity of patients after receiving Covid-19 vaccines. The skin test is designed to work in a similar fashion to the long-used skin test for tuberculosis or TB which produces a skin reaction on the forearm to evidence the level of T cell immunity in individuals exposed to TB.

Dr. Lederman, Tonix's CEO, concluded by noting that Covid-19 has taken a tremendous toll on people's lives and the world economy. "But we do not know if the current situation in the U.S. represents the end of the pandemic or if it is just a honeymoon," he added. "We are working hard to stay ahead of potential future problems. These potential problems include potential seasonal Fall and Winter rebounds in the number of new cases. For example, we may see increases in 'breakthrough COVID' in vaccinated people because the vaccines have limited duration of protection, or because new variants like Delta evade the vaccine protection. Tonix seeks to be a leader in the ongoing fight against Covid-19 and its sequelae and in pandemic preparedness generally."