Invivyd Announces General Alignment with FDA on Pathway to Potential EUA for VYD222 and Anticipated Follow-On Monoclonal Antibody Candidates Designed to Prevent COVID-19

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- *Unique, rapid development pathway for monoclonal antibodies (mAbs) using immunobridging via serum neutralizing titers could be enabled by previously generated clinical trial data from prototype antibody*
- *VYD222 and potential future Invivyd mAbs are planned to leverage this EUA pathway using consistent manufacturing platform and limited structural changes from proprietary prototype antibody ADG20 (adintrevimab)*
- *Company confirms plans to pursue rapid initiation of a VYD222 pivotal clinical trial using serum neutralizing titers as a correlate of protection (surrogate endpoint) to rapidly generate data for a potential VYD222 EUA submission*

WALTHAM, Mass., June 26, 2023 (GLOBE NEWSWIRE) -- Invivyd, Inc. (Nasdaq: IVVD), a clinical-stage biopharmaceutical company on a mission to protect the vulnerable from serious viral infectious diseases, today announced that it has reached general alignment with the U.S. Food and Drug Administration (FDA) on a pathway to potential emergency use authorization (EUA) for VYD222 and anticipated follow-on monoclonal antibody (mAb) candidates designed to prevent symptomatic COVID-19. The company plans to leverage the pathway, which includes the use of serum neutralizing titers as a correlate of protection (surrogate of clinical efficacy) in an immunobridging approach to a pivotal clinical trial of VYD222, to rapidly generate data to support a potential VYD222 EUA for the prevention of symptomatic COVID-19. Based on FDA feedback, the use of a correlate of protection in an immunobridging approach to a pivotal EUA-directed clinical trial may be a reasonable approach for a new mAb candidate when clinical trial data from a "prototype" mAb is available, provided that the new mAb candidate: (1) is similar to the prototype mAb such that it leverages a consistent manufacturing platform and has limited structural and functional differences, and (2) has supportive nonclinical data, such as favorable *in vitro* neutralization data against currently circulating SARS-CoV-2 variants.

Invivyd plans to leverage this immunobridging pathway to accelerate the clinical development of VYD222 and anticipated follow-on mAb candidates, with ADG20 (adintrevimab) or future proprietary mAbs serving as the prototype. The use of adintrevimab as the potential prototype mAb is proprietary to Invivyd and enabled by the robust safety data and clinically meaningful results from a global Phase 2/3 clinical trial of adintrevimab for the prevention of symptomatic COVID-19. VYD222 is a broadly neutralizing, half-life extended mAb candidate in development for the prevention of symptomatic COVID-19 in vulnerable populations, such as immunocompromised people. VYD222 was designed for broad activity and has previously demonstrated *in vitro* neutralizing activity against prior circulating SARS-CoV-2 variants and current variants of concern, including Omicron sublineages up to and through XBB.1.5.

In June 2023, the company announced positive initial safety and serum neutralizing titer data from the ongoing Phase 1 VYD222 clinical trial. Serum neutralizing titers are the same surrogate marker planned for use in the primary endpoint in a pivotal VYD222 clinical trial.

"We are very encouraged by the recent feedback from the FDA and appreciate their commitment to exploring alternative strategies to expedite the development of mAbs for the prevention of symptomatic COVID-19, such as the use of a correlate of protection as the primary endpoint in a pivotal clinical trial, a strategy that we are pleased to see further advance following the joint EMA-FDA workshop last December where the approach was discussed," said Dave Hering, chief executive officer of Invivyd. "Given our previous work developing adintrevimab and our platform-based approach to rapid mAb discovery, we believe we are one of few companies positioned to rapidly and serially generate data for potential EUA submission for next-generation mAb candidates for the prevention of symptomatic COVID-19. This potential pathway supports the company's vision and strategy of establishing a platform and stream of optimized anti-SARS-CoV-2 mAb candidates that can be deployed to keep pace with viral evolution and protect the vulnerable."

Invivyd continues activities to prepare for a VYD222 pivotal clinical trial and is pursuing a rapid initiation of that clinical trial in order to support a potential EUA submission. The company also continues to engage with global regulatory authorities regarding the VYD222 clinical development program.

About the Phase 1 Clinical Trial of VYD222

The ongoing VYD222 Phase 1 clinical trial is a randomized, blinded, placebo-controlled, dose-ranging trial that will evaluate the safety, pharmacokinetics, tolerability, and serum virus neutralizing activity of VYD222 in healthy adult volunteers (NCT05791318). The dose-ranging trial will evaluate three different doses of VYD222, each administered as a single IV push. All doses are designed to provide durability in the face of viral evolution and flexibility at the time of regulatory submission. In May 2023, Invivyd finished dosing all 30 participants in the trial; follow up is ongoing.

About VYD222

VYD222 is a broadly neutralizing, half-life extended monoclonal antibody (mAb) candidate in development for the prevention of symptomatic COVID-19 in vulnerable populations, such as immunocompromised people. Globally, there are millions of immunocompromised people, with an estimated 8-18 million in the U.S. alone, who may not adequately respond to COVID-19 vaccination, increasing their risk for severe outcomes from COVID-19. As of June 2023, there are no monoclonal antibodies authorized or approved in the U.S. for the prevention of symptomatic COVID-19.

VYD222 was designed for broad activity and has demonstrated *in vitro* neutralizing activity against previously circulating SARS-CoV-2 variants and current variants of concern, including Omicron sub-lineages up to and through XBB.1.5. VYD222 was engineered from adintrevimab, Invivyd's investigational mAb that has a robust safety data package and demonstrated clinically meaningful results in global Phase 2/3 clinical trials for both the prevention and treatment of COVID-19. The company believes the adintrevimab clinical data have the potential to support accelerated development of VYD222.

About the Phase 2/3 Clinical Trial of Adintrevimab for the Prevention of COVID-19 (EVADE)

EVADE was a multi-center, double-blind, placebo-controlled, randomized Phase 2/3 clinical trial of adintrevimab for post-exposure prophylaxis (PEP) and pre-exposure prophylaxis (PrEP) of symptomatic COVID-19 in SARS-CoV-2 naïve, unvaccinated individuals (NCT04859517). Eighty-eight sites randomized 2,582 participants in 8 countries. Eligible participants were adults (≥18 years) and adolescents (12 to <18 years) whose circumstances placed them at risk of acquiring SARS-CoV-2 infection. The PrEP cohort included participants whose advanced age (≥55 years) or health status placed them at risk for developing severe COVID-19 or COVID-19 complications, such as participants with chronic cardiopulmonary disease, diabetes, obesity, or an immune compromised state. The efficacy portion of EVADE was conducted during the emergence and global spread of SARS-CoV-2 variants Delta and Omicron BA.1/BA.1.1. Due to the marked differences in adintrevimab potency against these two variants, the EVADE trial provided a unique opportunity to assess the relationship between serum neutralizing titers and clinical protection against symptomatic COVID-19 in the absence of pre-existing SARS-CoV-2 immunity. The company believes it can leverage these data, along with its manufacturing platform, to support the accelerated development of VYD222 and a stream of mAb candidates designed to keep pace with SARS-CoV-2 evolution and protect the vulnerable.

About Invivyd

Invivyd, Inc. (Nasdaq: IVVD) is a biopharmaceutical company on a mission to rapidly and perpetually deliver antibody-based therapies that protect evulnerable people from the devastating consequences of circulating viral threats, beginning with SARS-CoV-2. Invivyd's technology works at th intersection of evolutionary virology, predictive modeling, and antibody engineering, and is designed to identify high-quality, long-lasting antibodies with the potential to resist viral escape. The company is generating a robust pipeline of product candidates which could be used in prevention or treatment of serious viral diseases, starting with COVID-19 and expanding into influenza and other high-need indications. Visit https://invivyd.com/ to learn more.

Cautionary Note Regarding Forward Looking Statements

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. Words such as "anticipates," "believes," "could," "expects," "intends," "potential," "projects," and "future" or similar expressions (as well as other words or expressions referencing future events, conditions or circumstances) are intended to identify forward-looking statements. Forward-looking statements include statements concerning, among other things, the future of the COVID-19 landscape; the company's ongoing research and clinical development plans and the timing thereof, including with respect to the clinical development of VYD222; the possibility for VYD222 and anticipated follow-on mAb candidates to follow a potential development pathway for mAbs using immunobridging via serum neutralizing titers and previously generated clinical trial data from a prototype antibody; the company's plans to utilize adintrevimab as a prototype mAb to accelerate the clinical development of VYD222; the company's plans to pursue rapid initiation of a VYD222 pivotal clinical trial using serum neutralizing titers as a correlate of protection (surrogate endpoint) to rapidly generate data for a potential VYD222 EUA submission; the company's beliefs about its competitive position; the company's vision and strategy of establishing a platform and stream of optimized anti-SARS-CoV-2 mAb candidates that can be deployed to keep pace with viral evolution and protect the vulnerable; estimates regarding the size of the company's target patient populations and the potential market opportunity for its product candidates; the company's ability to rapidly and perpetually deliver antibody-based therapies that protect vulnerable people from the devastating consequences of circulating viral threats; the potential for VYD222 and other product candidates to be high-quality, long-lasting antibodies with the potential to resist viral escape; the company's plans to generate a robust pipeline of product candidates which, if authorized or approved, could be used in prevention or treatment of serious viral diseases, starting with COVID-19 and expanding into influenza and other high-need indications; and other statements that are not historical fact. The company may not actually achieve the plans, intentions or expectations disclosed in the company's forward-looking statements and you should not place undue reliance on the company's forward-looking statements. These forward-looking statements involve risks and uncertainties that could cause the company's actual results to differ materially from the results described in or implied by the forward-looking statements, including, without limitation: the ability to gain complete alignment with the applicable regulatory authorities on the clinical trial design and development pathway for VYD222 and anticipated follow-on mAb candidates, including the use of an immunobridging pathway, and the timing thereof; whether adintrevimab is able to serve as a prototype mAb and the company is able to leverage previously generated adintrevimab clinical trial data in connection with the clinical development of VYD222 or potential future Invivyd mAb candidates; the timing and progress of the company's discovery, preclinical and clinical development activities, including the company's ability to rapidly initiate a VYD222 pivotal clinical trial and generate data for a potential VYD222 EUA submission; the ability of the company to generate and utilize tools to discover and develop a pipeline of antibodies to treat current and potential future SARS-CoV-2 variants; the impacts of the COVID-19 pandemic on the company's business and those of its collaborators, the company's clinical trials and its financial position; unexpected safety or efficacy data observed during preclinical studies or clinical trials; the predictability of clinical success of VYD222 or other product candidates based on neutralizing activity in preclinical studies; the risk that results of preclinical studies or clinical trials may not be predictive of future results in connection with current or future clinical trials; variability of results in models used to predict activity against SARS-CoV-2 variants of concern; clinical trial site activation or enrollment rates that are lower than expected; changes in expected or existing competition; changes in the regulatory environment; the uncertainties and timing of the regulatory approval process, including the outcome of the company's discussions with regulatory authorities concerning its clinical trials and platform-based approach to development; whether VYD222 or any other product candidate or combination of candidates is able to demonstrate and sustain neutralizing activity against predominant SARS-CoV-2 variant(s); whether the company is able to establish a platform and generate a stream of optimized anti-SARS-CoV-2 mAb candidates that can be deployed to keep pace with viral evolution and protect the vulnerable; whether VYD222 or other product candidates will be high-quality, long-lasting antibodies with the potential to resist viral escape; whether the company is able to successfully submit an EUA in the future, and the outcome of any such EUA submission; whether the company's research and development efforts will identify and result in safe and effective therapeutic options for infectious diseases other than COVID-19; and whether the company has adequate funding to meet future operating expenses and capital expenditure requirements. Other factors that may cause the company's actual results to differ materially from those expressed or implied in the forward-looking statements in this press release are described under the heading "Risk Factors" in the company's Annual Report on Form 10-K for the year ended December 31, 2022 filed with the Securities and Exchange Commission (the "SEC"), and in the company's other filings with the SEC, and in its future reports to be filed with the SEC and available at www.sec.gov. Such risks may be amplified by the impacts of the COVID-19 pandemic. Forward-looking statements contained in this press release are made as of this date, and Invivyd undertakes no duty to update such information whether as a result of new information, future events or otherwise, except as required under applicable law.

This press release contains hyperlinks to information that is not deemed to be incorporated by reference in this press release.

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