Invivyd Announces Positive Full Phase 1/2 Clinical Data for VYD2311, a Next Generation COVID-19 Monoclonal Antibody for Potential Use as a Non-Vaccine Preventative and for Treatment of Active Infection

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- *Attractive safety profile demonstrated across all dosing cohorts and routes of administration (IV, SC, and IM); all reported adverse events (AEs) deemed unrelated or classified as mild to moderate and largely related to injection site and infusion reactions with no serious or severe adverse events observed*
- *Following a single dose, serum concentrations of VYD2311 remained high at six months with an observed half-life of the IM dose route having the longest duration at 76.0 (CI: 68.5 – 90.7) days*
- *Comprehensive dose modeling of VYD2311 sVNA titers (submitted to FDA and under preparation for publication) indicates possible strong protection from symptomatic COVID-19 achievable via IM dosing on a long interval (months to quarters and beyond)*
- *Type C meeting scheduled with FDA for early Q3 to discuss registration-directed next steps for the VYD2311 program and overall approval pathway for Invivyd COVID-19 monoclonal antibodies*

WALTHAM, Mass., June 26, 2025 (GLOBE NEWSWIRE) -- Invivyd, Inc. (Nasdaq: IVVD), today announced full Phase 1/2 clinical data for VYD2311, a next-generation monoclonal antibody (mAb) candidate designed to prevent and treat COVID-19.

VYD2311 builds on the success of Invivyd's first-generation mAb, pemivibart, which received emergency use authorization (EUA) from the U.S. Food and Drug Administration (FDA) for the pre-exposure prophylaxis (prevention) of COVID-19 in certain adults and adolescents (12 years of age and older weighing at least 40 kg) who have moderate to-severe immune compromise. VYD2311 is 99%+ structurally identical to predicate antibodies adintrevimab and pemivibart, and represents the result of a technologically enabled, directed change in antibody sequence and spike protein target engagement uniquely accessible via Invivyd's technology platform. These subtle but critical molecular changes for VYD2311 confer an increase in in vitro potency and a differentiated resistance profile compared to pemivibart, with corresponding potential improvements in clinical profile and accessibility, if approved. VYD2311 is now the third mAb from Invivyd to undergo randomized clinical trial evaluation while retaining a near-identical molecular structure and target binding site on the SARS-CoV-2 spike protein, a feature of Invivyd's platform designed to provide vulnerable populations, healthcare professionals (HCPs), and regulatory authorities with a steady stream of high-assurance, minimally altered mAbs sufficient to navigate natural SARS-CoV-2 evolution rapidly with a non-vaccine approach.

The Phase 1/2 study of VYD2311 was a randomized, double-blind, first-in-human clinical trial evaluating the safety and clinical pharmacokinetic (PK) profile of VYD2311 in 40 subjects across multiple routes of administration (ROAs) and dose levels for a single dose, and includes VYD2311 dosed intravenously (IV), intramuscularly (IM), and subcutaneously (SC) in four cohorts of 10 participants each, randomized 8:2 to receive drug or placebo. This range of ROAs and doses was tested to provide maximum flexibility in designing registrational pathways for both COVID-19 prophylaxis and treatment, while retaining a high barrier to resistance in the form of doses expected to accommodate significant evolutionary changes in SARS-CoV-2 viruses.

VYD2311 was well tolerated with all adverse events (AEs) considered mild to moderate in severity with no serious or severe AEs reported. All AEs were deemed unrelated to study drug, or as expected and largely related to injection site erythema, injection site pain, injection site swelling, headache, dizziness, and infusion-related reactions, one of which (Grade 2) required an infusion interruption and was later restarted without any further reaction.

A formal estimate of in vivo half-life based on full Phase 1/2 clinical trial data confirmed the long half-life of VYD2311. At six months (end of study follow-up), serum concentrations of VYD2311 remained high and were observed to be substantially greater than that of pemivibart. Specifically, half-life estimates by cohort ranged from 61 days (high dose IV) to 76 days (IM) as compared to pemivibart estimated half-life of 49 days. VYD2311's long half-life could allow meaningful, long-term protection from symptomatic disease, potentially over multiple quarters, which is expected to be more durable than a COVID-19 vaccine, given rapid waning of protective benefit. High dose IV administration could similarly provide very long-term follow-up viral suppression in a COVID-19 treatment use case.

In addition to assessing safety and tolerability of VYD2311 across the various ROAs, a comprehensive dose modeling analysis was conducted to support development discussions with FDA and other global regulators about a rational dosing paradigm for VYD2311 and follow-on COVID-19 mAbs. A Cox model analysis was employed using data from Invivyd's recent CANOPY Phase

3 clinical trial for pemivibart, incorporating both serum virus neutralizing antibody (sVNA) titers and long-term clinical efficacy data to provide a robust foundation on which to reevaluate titer thresholds used to define efficacy for immunobridging purposes for both immunocompetent and immunocompromised (IC) individuals.

The VYD2311 dose modeling strategy contemplated a range of doses for IV up to 4500 mg, doses for IM up to 1000 mg, and doses for SC up to 750 mg. The results of this most recent analysis align well with prior published estimates of relationships between sVNA titers and observed clinical efficacy across multiple COVID-19 mAbs. Key findings of Invivyd's updated dose modeling analysis include:

- **Robust Modeled Protective Efficacy**: All dosing routes and doses assessed yielded modeled efficacy rates that appear to eclipse estimated contemporary rates of COVID-19 vaccine protection for both IC and non-IC individuals. Notably, IM and SC dosing every three months reflected robust efficacy for both IC and non-IC individuals and such routes could simplify and scale administration, improving convenience.
- **IM Dosing Comparable Performance to IV for Prevention**: Modeling data indicate that IM administration can offer efficacy comparable to high dose IV dosing. Critically, the IM route could eliminate the need for IV infrastructure - enhancing tolerability, accessibility, and convenience.
- **Very High Antiviral Titers Available via IV for Treatment of Active Infection**: Antiviral titers conferred by VYD2311 via IV to treat active infection are expected to substantially exceed the titers conferred by pemivibart and provide longer suppression of virus compared to pemivibart, and would seem to meet the criteria previously suggested by the FDA as persuasive of expected treatment effect in prior correspondence to Invivyd.

"These data reinforce our confidence in VYD2311's potential to offer a highly effective, scalable, convenient, and accessible solution for COVID-19 prevention," said Dr. Mark Wingertzahn, SVP Clinical Development at Invivyd. "The safety profile, long half-life, and novel dosing strategies explored with VYD2311 not only build upon the well-established science for COVID-19 mAbs to achieve robust modeled efficacy targets but also align with our mission to provide non-vaccine mediated protection to those most at risk, including immunocompromised individuals, in a manner that integrates seamlessly into standard healthcare settings."

"The release of these VYD2311 data represent a critical moment in our mission to modernize infectious disease protection through direct monoclonal antibody prophylaxis," said Marc Elia, Chairman of the Board at Invivyd. "The central scientific challenge associated with developing SARS-CoV-2 mAbs is the virus' continuous evolution. We designed Invivyd to solve this challenge not just by making best-in-class durable antibodies, but also by committing to serial iteration of those antibodies with minimal structural change so that viral evolution can be accommodated with rapid mAb development and authorization, while improving product profile whenever possible. Our proposed approach resembles the technological and regulatory approach long used for vaccines, but rather than delivering pieces of pathogen in vaccine form with its associated challenges, we propose to offer the natural, high efficacy benefit of mAb technology with a similar regulatory framework, leveraging surrogate endpoints based on clinical wisdom and common sense, all for the benefit of Americans in need. We are looking forward to discussing with the new FDA our next steps for providing gold standard options to prevent and treat SARS-CoV-2 infection."

Invivyd plans to discuss approval pathways for VYD2311 and follow-on COVID-19 mAbs with the FDA early in the third quarter of 2025, and expects to announce additional information about the VYD2311 program throughout 2025. Invivyd expects those discussions will include approval pathways for treatment of active COVID-19 and prophylaxis for vulnerable populations including the elderly, the immunocompromised, and pediatric populations including neonates and infants.

About VYD2311
VYD2311 is a novel monoclonal antibody (mAb) candidate being developed for COVID-19 to continue to address the urgent need for new prophylactic and therapeutic options. The pharmacokinetic profile and antiviral potency of VYD2311 may offer the ability to deliver clinically meaningful titer levels through more patient-friendly means such as an intramuscular route of administration.

VYD2311 was engineered using Invivyd's proprietary integrated technology platform and is the product of serial molecular evolution designed to generate an antibody optimized for neutralizing contemporary virus lineages. VYD2311 leverages the same antibody backbone as pemivibart, Invivyd's investigational mAb granted emergency use authorization in the U.S. for the pre-exposure prophylaxis (PrEP) of symptomatic COVID-19 in certain immunocompromised patients, and 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 the prevention and treatment of COVID-19.

About PEMGARDA
PEMGARDA® (pemivibart) is a half-life extended investigational monoclonal antibody (mAb). PEMGARDA was engineered from adintrevimab, Invivyd's investigational mAb that has a robust safety data package and provided evidence of clinical efficacy in global Phase 2/3 clinical trials for the prevention and treatment of COVID-19. PEMGARDA has demonstrated in vitro neutralizing activity against major SARS-CoV-2 variants, including JN.1, KP.3.1.1, XEC and LP.8.1. PEMGARDA targets the SARS-CoV-2 spike protein receptor binding domain (RBD), thereby inhibiting virus attachment to the human ACE2 receptor on host cells.

PEMGARDA (pemivibart) injection (4500 mg), for intravenous use is an investigational mAb that has not been approved, but has been authorized for emergency use by the U.S. FDA under an EUA for the pre-exposure prophylaxis (prevention) of COVID-19 in adults and adolescents (12 years of age and older weighing at least 40 kg) who have moderate-to-severe immune compromise due to certain medical conditions or receipt of certain immunosuppressive medications or treatments and are unlikely to mount an

adequate immune response to COVID-19 vaccination. Recipients should not be currently infected with or have had a known recent exposure to an individual infected with SARS-CoV-2.

PEMGARDA is not authorized for use for treatment of COVID-19 or post-exposure prophylaxis of COVID-19. Pre-exposure prophylaxis with PEMGARDA is not a substitute for vaccination in individuals for whom COVID-19 vaccination is recommended. Individuals for whom COVID-19 vaccination is recommended, including individuals with moderate-to-severe immune compromise who may derive benefit from COVID-19 vaccinations, should receive COVID-19 vaccination. In individuals who have recently received a COVID-19 vaccine, PEMGARDA should be administered at least 2 weeks after vaccination.

Anaphylaxis has been observed with PEMGARDA and the PEMGARDA Fact Sheet for Healthcare Providers includes a boxed warning for anaphylaxis. The most common adverse reactions included systemic infusion-related reactions and hypersensitivity reactions, local infusion site reactions, and infusion site infiltration or extravasation. For additional information, please see the PEMGARDA full product Fact Sheet for Healthcare Providers, including important safety information and boxed warning.

To support the EUA for PEMGARDA, an immunobridging approach was used to determine if PEMGARDA may be effective for pre-exposure prophylaxis of COVID-19. Immunobridging is based on the serum virus neutralizing titer-efficacy relationships identified with other neutralizing human mAbs against SARS-CoV-2. This includes adintrevimab, the parent mAb of pemivibart, and other mAbs that were previously authorized for EUA. There are limitations of the data supporting the benefits of PEMGARDA. Evidence of clinical efficacy for other neutralizing human mAbs against SARS-CoV-2 was based on different populations and SARS-CoV-2 variants that are no longer circulating. Further, the variability associated with cell-based EC50 value determinations, along with limitations related to pharmacokinetic data and efficacy estimates for the mAbs in prior clinical trials, impact the ability to precisely estimate protective titer ranges. Additionally, certain SARS-CoV-2 viral variants may emerge that have substantially reduced susceptibility to PEMGARDA, and PEMGARDA may not be effective at preventing COVID-19 caused by these SARS-CoV-2 viral variants.

The emergency use of PEMGARDA is only authorized for the duration of the declaration that circumstances exist justifying the authorization of the emergency use of drugs and biological products during the COVID-19 pandemic under Section 564(b)(1) of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 360bbb-3(b)(1), unless the declaration is terminated or authorization revoked sooner. PEMGARDA is authorized for use only when the combined national frequency of variants with substantially reduced susceptibility to PEMGARDA is less than or equal to 90%, based on available information including variant susceptibility to PEMGARDA and national variant frequencies.

About Invivyd
Invivyd, Inc. (Nasdaq: IVVD) is a biopharmaceutical company devoted to delivering protection from serious viral infectious diseases, beginning with SARS-CoV-2. Invivyd deploys a proprietary integrated technology platform unique in the industry designed to assess, monitor, develop, and adapt to create best in class antibodies. In March 2024, Invivyd received emergency use authorization (EUA) from the U.S. FDA for a monoclonal antibody (mAb) in its pipeline of innovative antibody candidates. 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,” “estimates,” “intends,” “potential,” “predicts,” “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 company’s ongoing research and development activities, as well as future potential research and development efforts; the potential of VYD2311 as a mAb candidate designed to prevent and treat COVID-19; expectations regarding the half-life and clinical profile of VYD2311, and the potential benefits thereof; the design of Invivyd’s platform to provide vulnerable populations, HCPs, and regulatory authorities with a steady stream of high-assurance, minimally altered mAbs sufficient to navigate natural SARS-CoV-2 evolution rapidly; the anticipated advantages of the range of ROAs and doses tested in the VYD2311 Phase 1/2 clinical trial, including the expected benefits of each of the SC, IM and IV ROAs; the potential of VYD2311 to offer a highly effective, scalable, convenient, and accessible solution for COVID-19 prevention; the expected advantages of VYD2311 over COVID-19 vaccines; Invivyd’s goals to provide non-vaccine mediated protection against COVID-19 and modernize infectious disease protection through direct mAb prophylaxis; Invivyd’s commitment to serial iteration of COVID-19 mAbs; the company’s regulatory plans and the timing thereof, including expectations related to Invivyd’s engagement with regulators, development discussions, and potential regulatory pathways for VYD2311 and follow-on COVID-19 mAbs; anticipated future announcements about the VYD2311 program, and the timing thereof; the potential of PEMGARDA as a mAb for pre-exposure prophylaxis (prevention) of COVID-19 in certain adults and adolescents who have moderate-to-severe immune compromise; the company’s devotion to delivering protection from serious viral infectious diseases, beginning with SARS-CoV-2; 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 timing, progress and results of the company’s discovery, preclinical and clinical development activities; the risk that results of nonclinical studies or clinical trials may not be predictive of future results, and interim data are subject to further analysis; unexpected safety or efficacy data observed during preclinical studies or clinical trials; the predictability of clinical success of the company’s product candidates

based on neutralizing activity in nonclinical studies; potential variability in neutralizing activity of product candidates tested in different assays, such as pseudovirus assays and authentic assays; variability of results in models and methods used to predict activity against SARS-CoV-2 variants; whether the epitope that VYD2311 and pemivibart targets remains structurally intact; whether the company's product candidates are able to demonstrate and sustain neutralizing activity against major SARS-CoV-2 variants, particularly in the face of viral evolution; whether Invivyd is able to deliver a steady stream of high-assurance, minimally altered mAbs sufficient to navigate natural SARS-CoV-2 evolution rapidly; the ability to gain alignment with the applicable regulatory authorities on the clinical trial designs and regulatory pathways for VYD2311 and follow-on COVID-19 mAbs, and the timing thereof; changes in the regulatory environment; uncertainties related to the regulatory authorization or approval process, and available development and regulatory pathways; clinical trial site activation or enrollment rates; how long the EUA granted by the FDA for PEMGARDA will remain in effect and whether the EUA is revised or revoked by the FDA; the ability to maintain a continued acceptable safety, tolerability and efficacy profile of any product candidate following regulatory authorization or approval; the company's ability to maintain and expand sales, marketing and distribution capabilities to successfully commercialize PEMGARDA; changes in expected or existing competition; the company's reliance on third parties; complexities of manufacturing mAb therapies; macroeconomic and political uncertainties; the company's ability to continue as a going concern; 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, 2024 and the company's Quarterly Report on Form 10-Q for the quarter ended March 31, 2025, each filed with the Securities and Exchange Commission (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. 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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