Invivyd Announces Positive Phase 1/2 Clinical Data for VYD2311, a Monoclonal Antibody Designed to be a Superior Alternative to COVID-19 Vaccination for the Broad Population

February 3, 2025

- *Recruitment completed and all doses administered for VYD2311 ongoing Phase 1/2 clinical trial (40 subjects) evaluating 3 routes of administration*
- *Phase 1/2 clinical data for VYD2311 to date are positive for both safety and pharmacokinetics, and are supported by antiviral activity data from Invivyd's standard virologic assessments*
    - *Pooled, blinded adverse events (AEs) to date are mild or moderate and thus far deemed unrelated to study drug or largely related to injection site reaction or infusion reactions*
    - *As of Day 65, serum concentrations remain high with half-life not yet reached, indicating potential long clinical dosing interval*
    - *In vitro neutralization potency of VYD2311 assessed across contemporary SARS-CoV-2 variants tested shows an average 17-fold greater neutralization potency than pemivibart*
- *Phase 1/2 clinical data, combined with antiviral assessment and COVID-19 antiviral correlate of protection data, including Invivyd's Phase 3 CANOPY clinical trial data for pemivibart, support a potential clinical profile for VYD2311 with superior efficacy, safety, and durability to COVID-19 vaccines:*
    - *Stronger protection (70-90%) from symptomatic COVID-19 disease*
    - *Less frequent (e.g. once- or twice-annual) intramuscular or subcutaneous dosing*
    - *More favorable safety and tolerability and, since VYD2311 is not a vaccine, no activation of subject immune systems*
- *Profile also suitable as a potential novel, potent, long-acting COVID-19 treatment option*

WALTHAM, Mass., Feb. 03, 2025 (GLOBE NEWSWIRE) -- Invivyd, Inc. (Nasdaq: IVVD) today announced positive data from its ongoing Phase 1/2 clinical trial of VYD2311, Invivyd's novel monoclonal antibody (mAb) candidate designed to be a superior alternative to COVID-19 vaccination for the broad population as frontline protection in a convenient form, as well as to provide a novel, potent, long-acting option for the treatment of COVID-19.

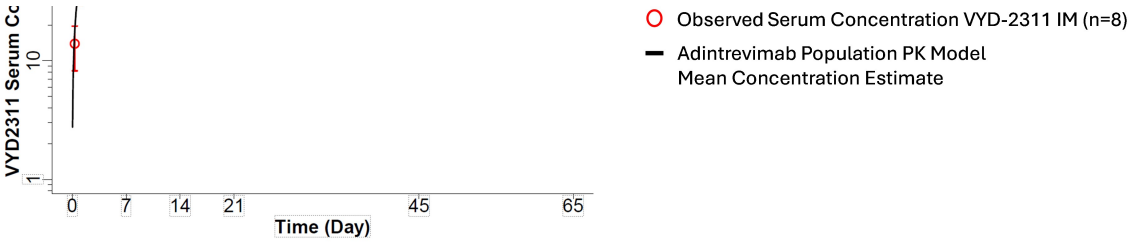
COVID-19 in 2024 caused approximately 59,000[1] deaths, 665,000[1] hospitalizations, and growing burden of Long COVID over time, despite broadly available and utilized vaccine boosts and small molecule therapy. The initial Phase 1/2 data support VYD2311's potential as a more effective and convenient option to manage this deadly disease.

Invivyd's ongoing randomized, double-blind, Phase 1/2 clinical trial is evaluating the safety and clinical pharmacokinetic (PK) profile of VYD2311 in 40 subjects across multiple routes of administration and dose levels for a single dose, and includes VYD2311 dosed intravenously (IV), intramuscularly (IM), and subcutaneously (SC) in four cohorts of 10 patients each, randomized 8:2 to receive drug or placebo. The Phase 1/2 clinical trial has fully enrolled, and all planned doses have been administered, with only long-term follow-up remaining.

While the Phase 1/2 trial remains blinded, all pooled, blinded adverse events (AEs) identified to date across all arms remain mild to moderate and largely confined to typical injection site reactions or infusion reactions.

A formal estimate of in vivo half-life is not yet available for VYD2311 given the long apparent half-life thus far. As of Day 65, serum concentrations remain high and represent a potential substantial increase in observed half-life of VYD2311 relative to pemivibart. Analysis for the IM cohort (the most advanced cohort in time) is tracking generally with the PK profile of adintrevimab, a previous Invivyd mAb with an estimated in vivo half-life of 139 days, as depicted in Figure 1 below. PK analysis of VYD2311 intravenous and subcutaneous cohorts at earlier timepoints, at either similar doses subcutaneously or higher doses intravenously, are similarly and encouragingly tracking close to the estimated curves for adintrevimab thus far.

Figure 1: Comparison of VYD2311 Measured Serum Concentration and Modeled Adintrevimab Concentration at Same Timepoints



In vitro neutralization data generated continuously on VYD2311 as part of Invivyd's industrial virology efforts demonstrate an average potency improvement for VYD2311 of approximately 17-fold compared to pemivibart, which is a benefit that is directly translatable into either an equivalent reduction in dose relative to PEMGARDA™ (pemivibart), or a corresponding increase in antiviral activity relative to PEMGARDA at equivalent doses.

Taken together, these VYD2311 safety, PK, and virology data, along with the data from Invivyd's CANOPY Phase 3 clinical trial for pemivibart[2] and other prior mAb pre-exposure prophylaxis studies[3], predict an attractive clinical protective profile of VYD2311, especially relative to COVID-19 vaccination, including likely highly protective titers of VYD2311 for up to six months or a year or more following a single dose. Shorter dosing intervals (e.g., quarterly or semi-annual) via either IM injection by a healthcare provider or at home via SC self-administration may be attractive for immunocompromised persons or other populations who may benefit from higher serum virus neutralizing antibody (sVNA) titers and, therefore, higher protection, and who also do not wish to interact regularly with healthcare infrastructure to acquire protection from COVID-19. Further, IM administration or higher doses of VYD2311 via IV infusion may be an attractive profile for purposes of delivering maximum possible antiviral activity to patients in need of treating active COVID-19.

"We are thrilled with these Phase 1/2 data for VYD2311, which we designed for the profile we are seeing so far: a potent and long-lasting mAb with the potential to protect people with none of the well-understood limitations of COVID-19 vaccination, and which, if brought to market, we believe can meaningfully interrupt disease in a fashion that is difficult or impossible for COVID-19 vaccination to ever achieve," commented Marc Elia, Chairman of the Invivyd Board of Directors. Mr. Elia continued, "Use of prior mAbs has been constrained by virus evolution, but the science we see now from our platform technology allows us to move game-changing technology like VYD2311 to the center of managing this deadly and pervasive virus. We look forward to collaborating with the U.S. FDA as we work to advance this important medicine to populations at highest risk of COVID-19."

"Last year, while sadly not broadly appreciated, more Americans died of COVID-19 than of breast cancer, and the growth in the long-term damage caused by COVID-19 (Long Covid) continues to mount in this endemic, mass disabling phase of our experience with SARS-CoV-2. Tens of millions of Americans remain at risk despite using serial boosts of vaccines that give short and modest protection from disease. While we are proud of our growing PEMGARDA business serving certain immunocompromised persons, we are seeking to maximize the medical and social impact of Invivyd's transformational science. Deploying a new protective mAb in the future that has the convenience and scalability of current vaccine boosts but with substantially more attractive protection, safety, and durability would be a massive step change in medical value for millions of Americans in need," said Tim Lee, Chief Commercial Officer of Invivyd.

VYD2311 was discovered via Invivyd technology that performs directed evolution of predicate antibodies toward higher potency against more contemporary SARS-CoV-2 virus lineages and has a highly similar epitope as parent molecule pemivibart and grandparent molecule adintrevimab, which epitope has been genetically and structurally stable over countless virus variants since the emergence of Omicron phylogeny virus.

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 and XEC. 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 events (all grades, incidence ≥2%) observed in participants who have moderate-to-severe immune compromise treated with PEMGARDA included systemic and local infusion-related or hypersensitivity reactions, upper respiratory tract infection, viral infection, influenza-like illness, fatigue, headache, and nausea. 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.

References

[1] From October 7, 2023, through September 28, 2024, the 2023-2024 respiratory season; hospitalizations calculated by Invivyd based on 334.9 million U.S. Census Bureau estimate of U.S. population size. Calculations based on cumulative rate for each disease state taken from the September 28, 2024, data point. References: CDC. RESP-NET. Accessed January 16, 2025. https://www.cdc.gov/resp-net/dashboard/?CDC; CDC. COVID Data Tracker. Accessed January 16, 2025. https://covid.cdc.gov/covid-data-tracker/#trends_weeklydeaths_select

[2] MedRxiv. Accessible here: https://www.medrxiv.org/content/10.1101/2024.11.11.24317127v1

[3] New England Journal of Medicine. Accessible here: Intramuscular AZD7442 (Tixagevimab–Cilgavimab) for Prevention of Covid-19 | New England Journal of Medicine; 2. NATURE Communications. Accessible here: Monoclonal antibody levels and protection from COVID-19 | Nature Communications

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 designed to be a superior alternative to COVID-19 vaccination for the broad population, and to provide a novel, potent, long-acting COVID-19 treatment option; the potential clinical profile of VYD2311 with respect to efficacy, safety, and durability; expectations related to the potential half-life, potency, clinical dosing intervals, and routes of administration of VYD2311; expectations regarding the COVID-19 landscape, beliefs about the limitations of current therapies for COVID-19, and the potential of Invivyd's platform technology to contribute to managing COVID-19; the company's expectation to collaborate with

the U.S. FDA to advance VYD2311; the company's goal to maximize the medical and social impact of its transformational science; the company's ongoing industrial virology effort; 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; the ability to gain alignment with the applicable regulatory authorities on the clinical trial design and development pathway for VYD2311, 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; 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, 2023 and the company's Quarterly Report on Form 10-Q for the quarter ended September 30, 2024, 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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