



## Invivyd Phase 3 Long-Term Exploratory Clinical Efficacy Data Shows PEMGARDA™ (pemivibart) Provided Substantial Protection from Symptomatic COVID-19 Versus Placebo Over Six Months of Follow-Up, With No Additional Doses, In Immunocompetent Participants

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- Following strong protection (84% relative risk reduction versus placebo) demonstrated through month 6 with pemivibart, CANOPY clinical trial participants were followed for an additional six-month period (months 7-12), with no additional doses, to assess safety and efficacy as drug concentrations declined over time
- In the six-month off-drug follow-up period (months 7-12), substantially reduced concentrations of PEMGARDA reduced the risk of symptomatic COVID-19 by 64% compared to placebo in an immunocompetent adult population, for total twelve-month risk reduction of 76% following two initial pemivibart doses (nominal  $p < 0.0001$ )
- Months 7-12 follow-up period included the U.S. summer KP.3 and KP.3.1.1 dominant wave, per CDC surveillance
- No new safety observations occurred months 7-12
- Across all 12 months of the CANOPY clinical trial, Cohort B placebo arm participants experienced an 18% rate of PCR-confirmed symptomatic COVID-19, excluding reinfections, indicative of continued, widespread, uncontrolled virus transmission in the U.S.

WALTHAM, Mass., Oct. 29, 2024 (GLOBE NEWSWIRE) -- Invivyd, Inc. (Nasdaq: IVVD), a biopharmaceutical company devoted to delivering protection from serious viral infectious diseases, today announced positive 12-month exploratory clinical efficacy data from the company's ongoing CANOPY Phase 3 clinical trial of pemivibart, a half-life extended investigational monoclonal antibody (mAb), for the pre-exposure prophylaxis (PrEP) of COVID-19.

The exploratory clinical efficacy data from follow-up months 7-12 in CANOPY Cohort B, a placebo-controlled cohort of immunocompetent individuals at risk for symptomatic COVID-19 disease due to regular unmasked face-to-face indoor interactions, showed a relative risk reduction (RRR) of 64% in the pemivibart arm compared to placebo in the likelihood of trial participants contracting confirmed symptomatic COVID-19. Continued protection over this follow-up period, absent continued dosing, was a prespecified exploratory endpoint and, added to initial 180-day clinical efficacy observations, generated an overall 12-month protection rate of 76% following two doses of pemivibart (administered on Days 1 and 90), nominally significant at  $< 0.0001$ . Clinical efficacy data are displayed in the table below.

	Placebo Arm			Pemivibart Arm			RRR***	Nominal p value
	Subjects	COVID-19 Cases	Attack Rate	Subjects	COVID-19 Cases	Attack Rate		
<i>On-drug Period</i>								
0-6 months*	160	19	11.9%	317	6	1.9%	84%	<0.0001
<i>Long-term Follow-up Period Following Cessation of Dosing</i>								
0-9 months	160	20	12.5%	317	8	2.5%	80%	<0.0001
0-12 months	160	29	18.1%	317	14	4.4%	76%	<0.0001
7-12 months**	133	10	7.5%	289	8	2.8%	64%	0.0285

\* Period includes US JN.1 wave

\*\* Period includes US KP.3 and KP.3.1.1 wave

\*\*\* Relative risk reduction excludes deaths unrelated to COVID-19

Pemivibart has an estimated in vivo half-life of approximately 45 days, and pemivibart IC50 values against circulating viruses are tested routinely, allowing for the calculation of the average serum virus neutralizing antibody (sVNA) titer over time, the measure of how much antiviral activity pemivibart confers to treated participants. Previously published literature<sup>1</sup> indicates likely robust protection from symptomatic COVID-19 at sVNA titer levels well below the levels delivered by the authorized PEMGARDA (pemivibart) dosing regimen. In this updated CANOPY exploratory analysis, the 64% RRR (excluding deaths unrelated to COVID-19) that residual circulating pemivibart delivered versus placebo in months 7 through 12 occurred at calculated average titers of only approximately 7% of the average titers during the active dosing period. This was attributable to the expected decline in pemivibart serum concentrations following cessation of dosing, along with modest change to assessed pemivibart IC50 in the transition from the JN.1 dominant virus to the KP lineage dominant circulating viruses.

"Today's data underline our high confidence in the clinical benefit that mAbs like pemivibart can confer even at very low serum

concentrations and associated antiviral titers,” commented Robert Allen, Ph.D., Chief Scientific Officer of Invivyd. “Engineered mAbs are designed to confer a step change in protection compared to the protection possible from native immune response to infection and vaccination boosts<sup>2</sup>. We believe that the clinical risk reduction generated at such low titers in this CANOPY clinical trial follow-up, which builds on now longstanding published data, implies that the modest changes (less than ~10 fold change) in pemivibart IC50 observed against emerging variants are of questionable significance.”

“Our company’s goal is to provide high quality options for protection from SARS-CoV-2. Today’s exploratory clinical efficacy data update from our Phase 3 trial is critical, as it adds contemporary context to longstanding data showing strong protection from COVID-19 disease at relatively low sVNA titers with mAbs,” commented Marc Elia, Chairman of the Invivyd Board of Directors. “These consistent observations now span years and countless virus lineages and mutations, and, in toto, suggest that Invivyd, pending alignment with regulators, can develop and commercialize low-dose, high potency, long-acting mAbs that can have the same route of administration and system-friendliness as COVID-19 vaccine boosts, but with the goal of higher, more consistent, and longer-acting protection. Our current pipeline molecule, VYD2311, is currently in Phase 1 testing including an intramuscular (IM) administration in anticipation of executing against this exact goal.”

The safety profile of pemivibart over the 12-month study period was reassuring with no new trends or safety signals observed for treatment-emergent adverse events (TEAEs) or infusion-related reactions or hypersensitivity reactions since the disclosure of the 6-month CANOPY data. Over the 12 months, in Cohort A, an open-label single-arm cohort, the most common TEAEs (>5%) included upper respiratory tract infection (URTI) (10.1%), viral infection (8.8%), urinary tract infection (UTI) (5.6%), and influenza-like illness (5.2%). As previously disclosed, anaphylaxis was observed in 4 participants (0.6%) in Cohort A – 2 participants during the first infusion and 2 participants during the second infusion; two reactions were life-threatening, and all led to permanent discontinuation of pemivibart. Infusion-related reactions and hypersensitivity reactions within 24 hours of dosing pemivibart were observed in 8.2% and 3.9% of participants in Cohort A after the initial dose and redose, respectively, and were generally mild to moderate in severity. Over the 12 months, in Cohort B, the most common TEAEs in the pemivibart arm included viral infection (8.5%), URTI (8.5%), and influenza-like illness (5.7%), with higher percentages in the placebo arm. No participants developed anaphylaxis. Infusion-related reactions and hypersensitivity reactions within 24 hours of dosing pemivibart were observed in 1.3% and 2.5% of participants in Cohort B after initial dose and redose, respectively, and were all mild or moderate in severity. Serious Adverse Events (SAEs) occurring in >1 Cohort A participant included pneumonia (n=3), anaphylactic reaction (n=2), hypotension (n=2), pyelonephritis (n=2), syncope (n=2), and UTI (n=2). No SAEs occurred in >1 participant in either treatment arm in Cohort B. These data support that the safety profile for pemivibart remains consistent with the PEMGARDA Fact Sheet for Healthcare Providers and the known safety profile of other SARS-CoV-2-directed mAbs.

CANOPY Cohort B exploratory clinical efficacy results from months 7-12 provide data from reduced concentration of pemivibart and reduced sVNA titers in a contemporary immunocompetent population that had acquired prior immune exposure from either vaccination or natural infection and overlapped with the height of the Summer 2024 KP.3 and KP3.1.1 wave that saw a surge in COVID-19 cases nationwide in the U.S. By contrast, ancestral clinical trials of prior COVID-19 PrEP candidate mAbs were performed in populations naïve to vaccination or infection.

The months’ 7-12 CANOPY Cohort B clinical efficacy exploratory data announced today complement the 180-day clinical efficacy exploratory data demonstrating potential signals of clinical protection from symptomatic COVID-19 shared previously. The company expects the full data set to be provided in an upcoming scientific publication.

### **About Invivyd**

Invivyd, Inc. (Nasdaq: IVVD) is a biopharmaceutical company devoted to delivering protection from serious viral infectious diseases, beginning with SARS-CoV-2. The company’s proprietary INVYMAB™ platform approach combines state-of-the-art viral surveillance and predictive modeling with advanced antibody engineering. INVYMAB is designed to facilitate the rapid, serial generation of new monoclonal antibodies (mAbs) to address evolving viral threats. In March 2024, Invivyd received emergency use authorization (EUA) from the U.S. FDA for its first mAb in a planned series of innovative antibody candidates. Visit <https://invivyd.com/> to learn more.

### **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 a global Phase 2/3 clinical trial for the prevention and treatment of COVID-19. PEMGARDA has demonstrated in vitro neutralizing activity against major SARS-CoV-2 variants, including JN.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 events (all grades, incidence  $\geq 2\%$ ) 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 CANOPY**

The ongoing CANOPY Phase 3 clinical trial is designed to evaluate the safety and tolerability of pemivibart and to assess immunobridging from pemivibart to certain historical data from the company's previous Phase 2/3 clinical trial of adintrevimab (ADG20) for the prevention of symptomatic COVID-19 (EVADE). Additionally, there are pre-specified exploratory endpoints through three, six and twelve months to evaluate clinical efficacy of pemivibart compared to placebo in the prevention of RT-PCR-confirmed symptomatic COVID-19. The latest analysis from the Phase 3 CANOPY clinical trial includes 365-day data. The CANOPY clinical trial enrolled participants in two cohorts: Cohort A is a single-arm, open-label trial in adults who have moderate-to-severe immune compromise including complex underlying medical conditions. Cohort B is a randomized, placebo-controlled cohort that enrolled adults without moderate-to-severe immune compromise who are at risk of acquiring COVID-19 due to regular unmasked face-to-face interactions in indoor settings.

#### **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," "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 clinical development activities, as well as future potential research and clinical development efforts; the potential clinical benefit that mAbs like PEMGARDA (pemivibart) can confer, even at very low serum concentrations and associated antiviral titers; the possibility for Invivyd to develop and commercialize low-dose, high potency, long-acting mAbs with the same route of administration and system-friendliness as COVID-19 vaccine boosts, but higher, more consistent, and longer-acting protection; the company's expectation to provide a full data set from the CANOPY clinical trial in an upcoming scientific publication; 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; the design of the company's INVYMAB platform approach to facilitate the rapid, serial generation of new mAbs to address evolving viral threats; the company's plans for a series of innovative antibody candidates and its goals for pipeline molecule VYD2311; 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; the company's reliance on third parties with respect to virus assay creation and product candidate testing and with respect to its clinical trials; variability of results in models used to predict activity against SARS-CoV-2 variants; whether pemivibart, VYD2311, or any other product candidate is able to demonstrate and sustain neutralizing activity against major SARS-CoV-2 variants, particularly in the face of viral evolution; 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 company's ability to build and maintain sales, marketing and

distribution capabilities to successfully commercialize PEMGARDA; uncertainties related to the regulatory authorization or approval process, and available development and regulatory pathways for authorization or approval of the company's product candidates; the ability to maintain a continued acceptable safety, tolerability and efficacy profile of any product candidate following regulatory authorization or approval; changes in the regulatory environment; changes in expected or existing competition; the complexities of manufacturing mAb therapies; the company's ability to leverage its INVYMAB platform approach to facilitate the rapid, serial generation of new mAbs to address evolving viral threats; any legal proceedings or investigations relating to the company; 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 June 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](http://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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<sup>1</sup>Schmidt, et al. Antibody-Mediated Protection Against Symptomatic COVID-19 Can Be Achieved at Low Serum Neutralizing Titers. *Sci. Transl. Med.* 15, eadg2783 (2023); Stadler, et al. Monoclonal Antibody Levels and Protection From COVID-19, *Nat. Commun.*, 14:4545 (2023)

<sup>2</sup> <https://www.cdc.gov/acip/downloads/slides-2024-06-26-28/03-COVID-Link-Gelles-508.pdf>