Clinical Efficacy Endpoints from the Phase 3 CANOPY Study Evaluating Pemivibart for the Prevention of COVID-19

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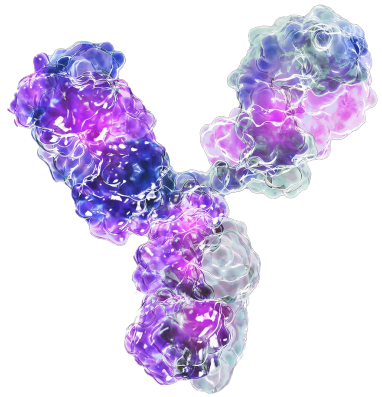
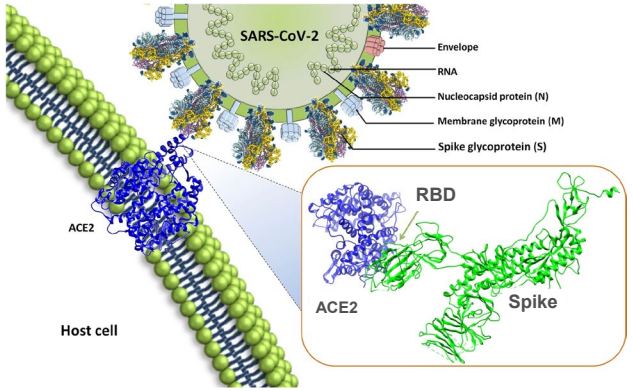
DISCLOSURES

- Pemivibart is an investigational product candidate that is not approved for use in any country. The safety and efficacy of pemivibart have not been established.
- This work was sponsored by Invivyd, Inc
- The following authors, Anna Holmes, Chloe Katz, Anne-Marie Phelan, Kazima Tosh, Yong Li, Deepali Gupta, Pamela Hawn, Kristin Narayan, and Mark Wingertzahn, are employees of Invivyd, Inc, and may own stock
- Myra Popejoy and Kathryn Mahoney were employees of Invivyd, Inc. at the time the study was conducted
- All relevant financial disclosures have been mitigated

PEMIVIBART (VYD222)



Half-life–extended mAb that has been issued an EUA by the FDA for pre-exposure prophylaxis of COVID-19 in certain adults and adolescents with moderate-to-severe immune compromise



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Binds to the spike protein receptor binding domain (RBD) of SARS-CoV-2, interfering with the virus's ability to infect human cells[1]

EVADE

Phase 2/3 clinical trial of adintrevimab for COVID-19 prevention

STAMP

Phase 2/3 clinical trial of adintrevimab for COVID-19 treatment

Engineered from adintrevimab (ADG20), a mAb candidate that demonstrated clinical efficacy against earlier SARS-CoV-2 variants in 2 previous clinical trials[2,3]

EUA, emergency use authorization; FDA, US Food and Drug Administration; mAb, monoclonal antibody.

1. Saxena SK, et al. *VirusDis*. 2020; 31:399-407. 2. Ison MG, et al. *Open Forum Infect Dis*. 2023;10:ofad279. 3. Ison MG, et al. *Open Forum Infect Dis*. 2023;10:ofad314.

A study to evaluate the efficacy and safety of pemivibart for prevention of COVID-19 (CANOPY)

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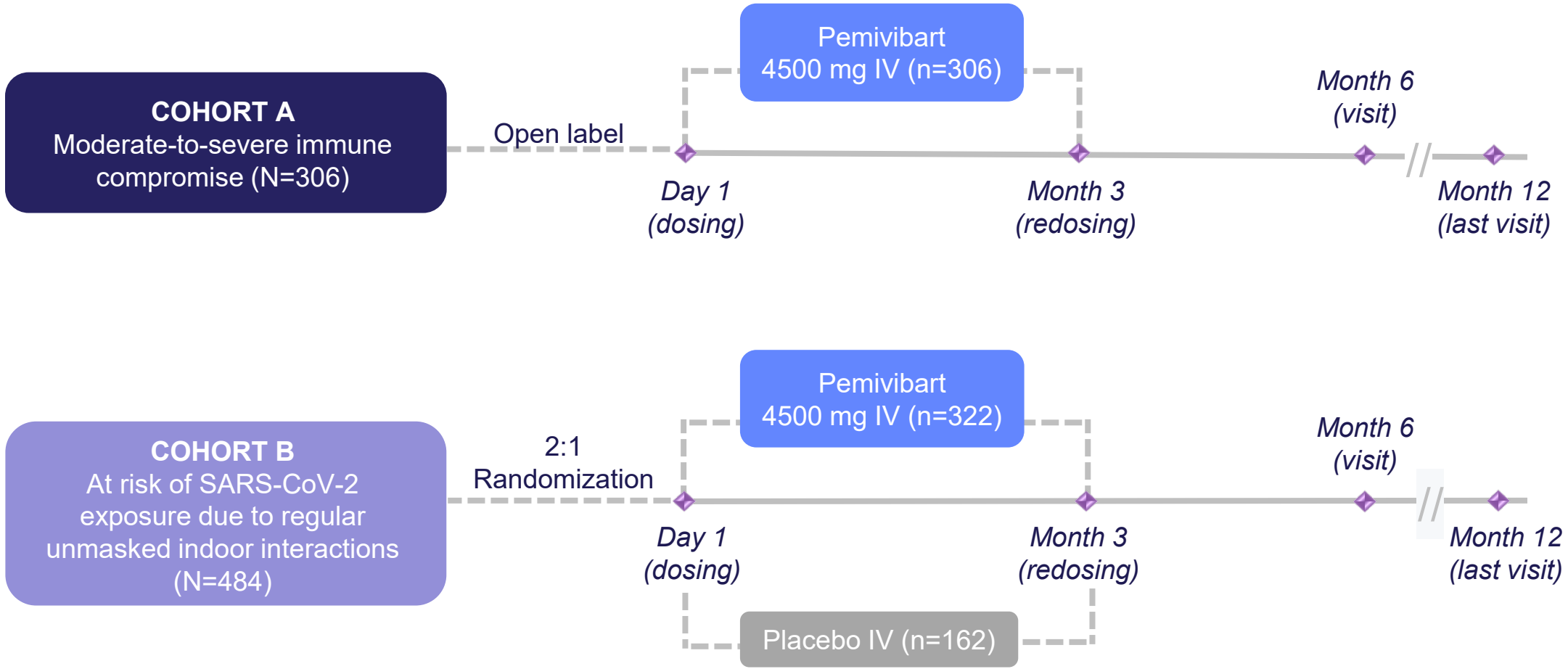
CANOPY: PHASE 3 CLINICAL TRIAL

CANOPY STUDY OVERVIEW



IV, intravenous.
ClinicalTrials.gov Identifier: NCT06039449.

STUDY OBJECTIVES

A study to evaluate the efficacy and safety of pemivibart for prevention of COVID-19 (CANOPY)

Cohort A primary objectives

- Evaluate protection against symptomatic COVID-19 based on sVNA titers against SARS-CoV-2 after receiving pemivibart using an immunobridging approach
- Evaluate the safety and tolerability of pemivibart in all treated participants

Cohort B primary objectives

- Evaluate the safety and tolerability of pemivibart compared with placebo in all treated participants

Additional objectives: Cohorts A and B

- Evaluate PK, ADA, and prevention of RT-PCR–confirmed symptomatic COVID-19

ADA, antidrug antibody; PK, pharmacokinetics; RT-PCR, reverse transcription polymerase chain reaction; sVNA, serum virus neutralization antibody.

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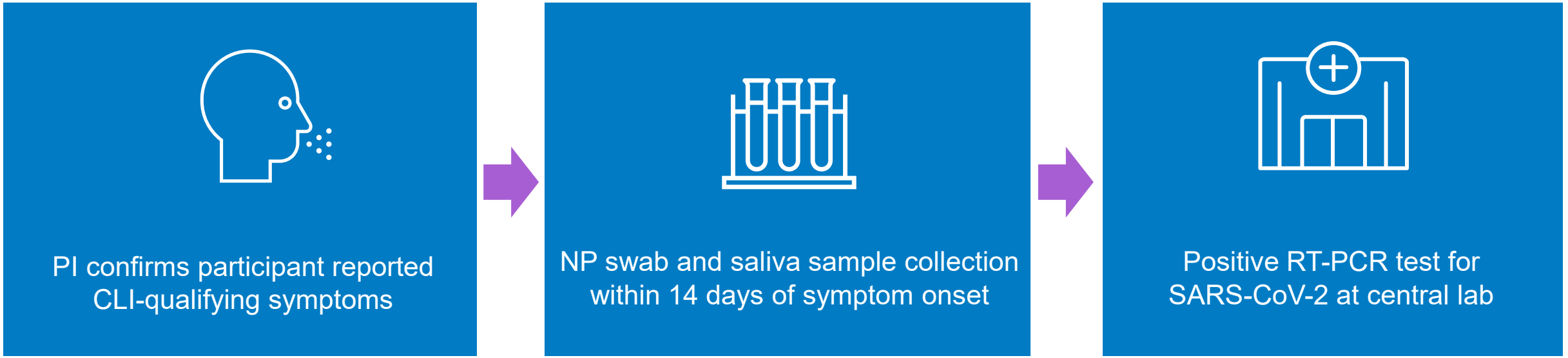
EXPLORATORY EFFICACY ENDPOINT
RT-PCR–confirmed symptomatic COVID-19

- Participants who presented with symptoms of COVID-19 were instructed to contact site study team and report to site within 2 days of symptom confirmation for collection of nasopharyngeal and saliva samples for central RT-PCR SARS-CoV-2 testing
- Information regarding duration and severity of COVID-19 symptoms was collected approximately 28 days after sample collection



- Positive central RT-PCR result for SARS-CoV-2 from NP swab, saliva sample, and/or NP swab for respiratory pathogen panel were included in the endpoint

CLI, COVID-like illness; NP, nasopharyngeal; PI, principal investigator; RT-PCR, reverse transcription polymerase chain reaction.
VYD222-PREV-001 protocol, version 4.0. April 15, 2024.

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BASELINE DEMOGRAPHICS AND CHARACTERISTICS

	Cohort A	Cohort B	
	Pemivibart (N=306)	Pemivibart (N=322)	Placebo (N=162)
Age, median (range), years	59 (22–83)	47.5 (18–84)	48 (19–78)
Age 18 to <55, n (%)	127 (41.5)	204 (63.4)	102 (63.0)
Age ≥55, n (%)	179 (58.5)	118 (36.6)	60 (37.0)
Age ≥65, n (%)	95 (31.0)	61 (18.9)	27 (16.7)
Age ≥75, n (%)	22 (7.2)	9 (2.8)	1 (0.6)
Female, n (%)	187 (61.1)	166 (51.6)	91 (56.2)
White, n (%)	262 (85.6)	201 (62.4)	108 (66.7)
Black, n (%)	37 (12.1)	94 (29.2)	48 (29.6)
Body mass index, median (range), kg/m^2	28.3 (16.8–61.2)	28.4 (17.7–55.7)	28.7 (17.4–56.6)
% participants receiving any prior COVID-19 vaccine, n (%)	269 (87.9)	189 (58.7)	100 (61.7)
No. of vaccines received, median (range)	5 (1–11)	3 (1–6)	3 (1–5)
Baseline serology, n (%)			
N protein positive	150 (49.0)	273 (84.8)	139 (85.8)
S protein positive	299 (97.7)	317 (98.4)	161 (99.4)

Invivyd, Inc. Data on file.

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BASELINE CHARACTERISTICS

Risk factors for progression to severe COVID-19

	Cohort A	Cohort B	
	Pemivibart (N=306)	Pemivibart (N=322)	Placebo (N=162)
Risk factor for COVID-19 disease progression, n (%)	306 (100)	213 (66.1)	100 (61.7)
Age ≥55 years	179 (58.5)	118 (36.6)	60 (37.0)
Obesity (BMI >30 kg/m^2)	116 (37.9)	129 (40.1)	65 (40.1)
Diabetes (Type 1 or 2)	54 (17.6)	29 (9.0)	15 (9.3)
Chronic kidney disease	31 (10.1)	1 (0.3)	2 (1.2)
Chronic lung disease	58 (19.0)	8 (2.5)	7 (4.3)
Cardiac disease	129 (42.2)	68 (21.1)	41 (25.3)
Solid organ transplant recipient	33 (10.8)	0	0
Other immunodeficiency due to underlying illness or immunosuppressant medication	306 (100)	4 (1.2)	1 (0.6)
Stroke or cerebrovascular disease	9 (2.9)	0	1 (0.6)
Substance use disorder	6 (2.0)	4 (1.2)	3 (1.9)

BMI, body mass index.
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MEDICAL HISTORY
Criteria for significant immunocompromise

Immunocompromising condition,[a] n (%)	Cohort A Pemivibart (N=306)
Taking immunosuppressive/immunomodulatory medications	202 (66.0)
Acute leukemia, chronic lymphocytic leukemia, non-Hodgkin lymphoma, or multiple myeloma	40 (13.1)
Moderate or severe primary immunodeficiency	37 (12.1)
Solid organ transplant recipient taking immunosuppressive therapy	33 (10.8)
Advanced HIV infection	27 (8.8)
Actively treated solid tumor or hematologic malignancy	20 (6.5)
CAR-T–cell therapy or hematopoietic stem cell transplant	0

CAR, chimeric antigen receptor.
[a]Participants could be included in more than 1 condition.
Invivyd, Inc. Data on file.

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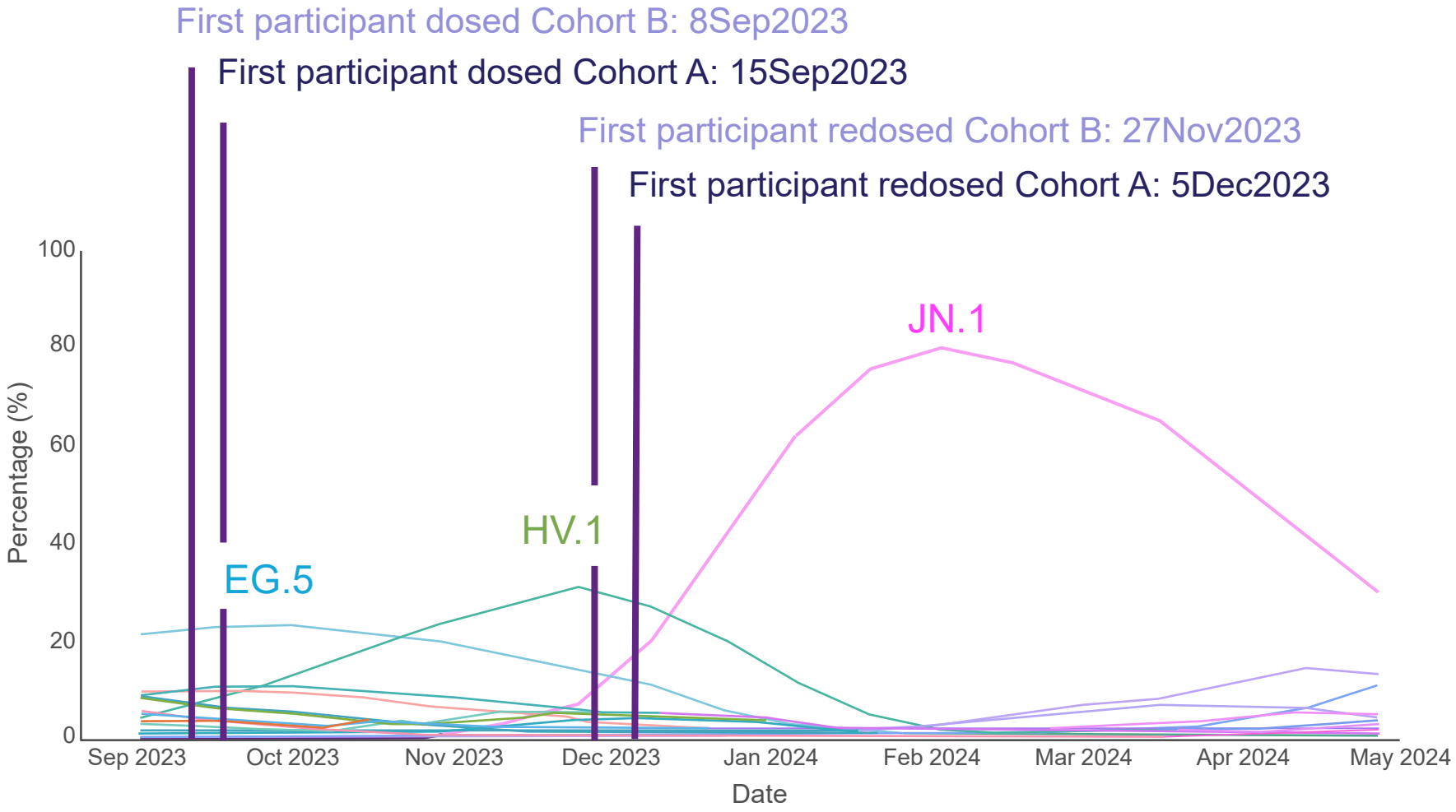
SARS-CoV-2 predominant variants during assessment period



CDC COVID Data Tracker. Available at: https://covid.cdc.gov/covid-data-tracker/#variant-proportions.

CDC, US Centers for Disease Control and Prevention.
Source: Invivyd Inc. Data on file and CDC.

INCIDENCE OF RT-PCR–CONFIRMED SYMPTOMATIC COVID-19, COVID-19–RELATED HOSPITALIZATIONS, AND ALL-CAUSE MORTALITY

Cohort B

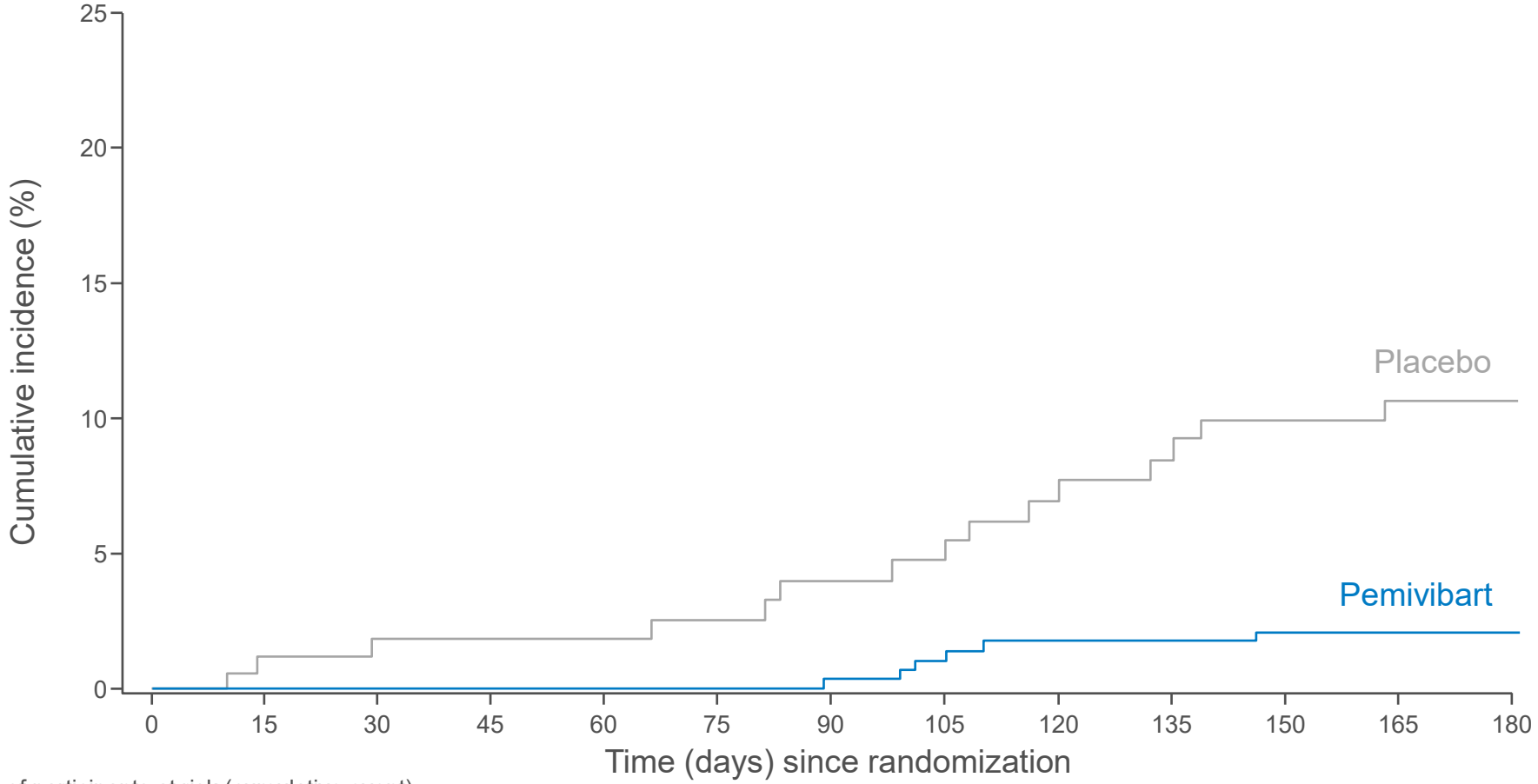
- Cohort B: randomized, placebo-controlled cohort without moderate-to-severe immunocompromise at risk of acquiring SARS-CoV-2 due to regular indoor, unmasked face-to-face interactions

	Through Day 180, n (%)	RRR (95% CI)	Nominal *P* value
Pemivibart (n=317)	6 (1.9)	–	–
Placebo (n=160)	19 (11.9)	84.1% (61, 94)	0.000061

- Exploratory clinical efficacy endpoint
- No COVID-19–related hospitalizations or deaths were observed in Cohort B

RRR, relative risk reduction; RT-PCR, reverse transcription polymerase chain reaction.
Invivyd, Inc. Data on file.

TIME TO EVENT (RT-PCR–CONFIRMED SYMPTOMATIC COVID-19) ANALYSIS
Cohort B



No. of participants at risk (cumulative event)

Placebo	160 (0)	158 (2)	154 (3)	143 (3)	137 (3)	135 (4)	132 (6)	128 (8)	125 (11)	122 (13)	120 (14)	119 (15)	119 (15)
Pemivibart	317 (0)	311 (0)	310 (0)	295 (0)	289 (0)	287 (0)	285 (1)	277 (4)	273 (5)	271 (5)	269 (6)	268 (6)	268 (6)

An 84% relative risk reduction of RT-PCR–confirmed symptomatic COVID-19 in Cohort B (immunocompetent population) with pemivibart treatment vs placebo

Participants who experienced symptomatic COVID-19 after receiving a COVID-19 vaccine during the study were censored at the time of vaccination for this analysis; 4 such cases in the placebo arm.
RT-PCR, reverse transcription polymerase chain reaction.

INCIDENCE OF RT-PCR–CONFIRMED SYMPTOMATIC COVID-19, COVID-19–RELATED HOSPITALIZATIONS, AND ALL-CAUSE MORTALITY

Cohort A

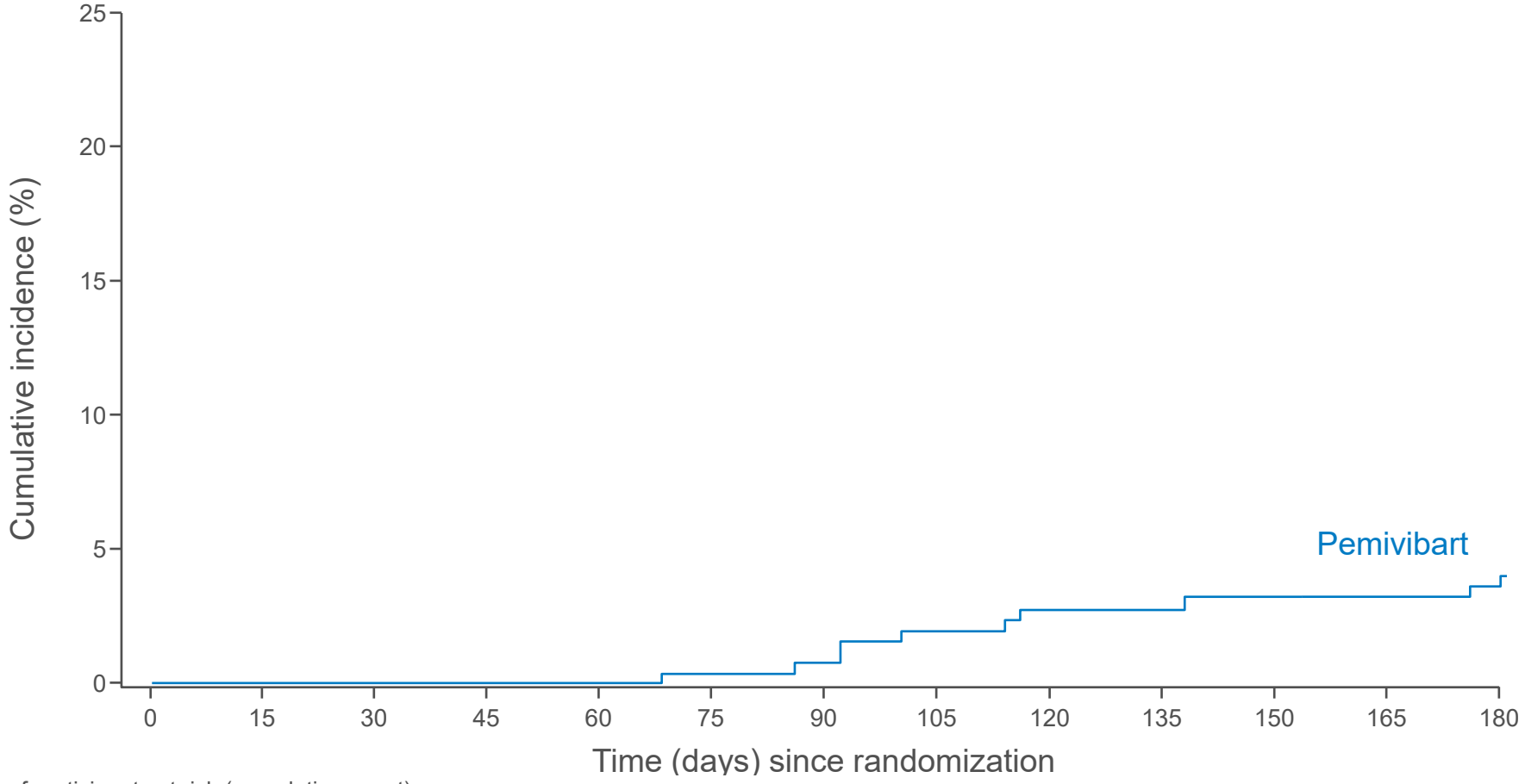
- Cohort A: single-arm, open-label cohort in adults with moderate-to-severe immunocompromise

Outcome through Day 180, n (%)	Pemivibart (N=298)
Composite RT-PCR–confirmed COVID-19	11 (3.7)
Symptomatic COVID-19	9 (3.0)
COVID-19–related hospitalizations	0
All-cause mortality[a]	2 (0.7)

- Exploratory clinical efficacy endpoint

[a]Two deaths occurred in Cohort A (1 by suicide, 1 by unknown cause).
RT-PCR, reverse transcription polymerase chain reaction.
Invivyd, Inc. Data on file.

TIME TO EVENT (RT-PCR–CONFIRMED SYMPTOMATIC COVID-19) ANALYSIS
Cohort A



No. of participants at risk (cumulative event)

Pemivibart	298 (0)	298 (0)	294 (0)	262 (0)	249 (0)	247 (1)	245 (2)	242 (5)	240 (7)	234 (7)	231 (8)	228 (8)	224 (10)

A low rate of RT-PCR–confirmed symptomatic COVID-19 (3.7%) in pemivibart-treated participants in Cohort A (significantly immunocompromised population) following 2 doses of pemivibart administered 3 months apart

Participants who experienced symptomatic COVID-19 after receiving a COVID-19 vaccine during the study were censored at the time of vaccination for this analysis; 1 such case occurred in these pemivibart-treated participants.
RT-PCR, reverse transcription polymerase chain reaction.

RT-PCR–CONFIRMED COVID-19 THROUGH 180 DAYS

Participant characteristics and case severity

	Cohort A	Cohort B	
	Pemivibart (N=11[a])	Pemivibart (N=6)	Placebo (N=19)
Age, median (range), years	55 (24–66)	53 (29–84)	50 (20–78)
Female, n (%)	8 (72.7)	5 (83.3)	12 (63.2)
Severity of COVID-19 illness, n (%)			
Mild	5 (45.5)	3 (50.0)	10 (52.6)
Moderate	4 (36.4)	3 (50.0)	8 (42.1)
Severe	0	0	1 (5.3)

- Severity of COVID-19–like illness (CLI) was assessed by participant self-assessment and classified as mild, moderate, or severe, considering the entire course of the disease from onset of symptoms through CLI Day 28 or resolution of symptoms, whichever is earlier
- Severity of COVID-19 was an exploratory endpoint

[a]Two deaths occurred in Cohort A (1 by suicide, 1 by unknown cause)

Invivyd, Inc. Data on file.

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EXPLORATORY ANALYSIS OF COVID-19 VARIANTS IN CANOPY

Confirmed infections through Day 180

- Targeted spike sequencing was attempted on RT-PCR–positive NP samples from confirmed events (positive saliva samples were not sequenced)
- Only samples with sufficient viral load were successfully sequenced
- Variants identified are consistent with predominant circulating lineages from September 2023 to May 2024, including the JN.1 wave in early 2024
- No unexpected IC_{50} shifts for variants identified in breakthrough cases; resistance analysis of these cases is ongoing

		Cohort A (pemivibart) event rate: 3.0%	Cohort B (pemivibart) event rate: 1.9%	Cohort B (placebo) event rate: 11.9%
Successful sequences/ # positive events		**5/9**	**0/6**	**13/19**
XBB*-related lineages	EG.5.1.1	–	–	1
	HV.1	–	–	1
	GS.4.1	–	–	1
	FL.1.5.1	–	–	1
	HV.1.5	–	–	1
	XBB.1.5.28	–	–	1
JN.1-related lineages	JN.1	5	–	6
	JN.1.28	–	–	1

Note: lineage is determined based off targeted spike sequence and NextStrain tool.
IC_{50}, half maximal inhibitory concentration; NP, nasopharyngeal; RT-PCR, reverse transcription polymerase chain reaction.
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SAFETY SUMMARY (THROUGH DAY 180)
Cohort A

- Adverse events occurred in 66.7% of participants
- Most TEAEs were mild or moderate, and the most common TEAEs (≥3.0%) were viral infection (7.8%), URTI (7.5%), ILI (4.2%), IRR (3.6%), and UTI (3.6%)
- Study drug–related TEAEs occurred in 11.1% of participants, and serious study drug–related TEAEs occurred in 0.7% of participants, with no study drug–related deaths
  - Study drug–related TEAEs led to study drug dosing interruption in 4.6% of participants and to study drug discontinuation in 2.3% of participants
- Possible symptoms of infusion-related or hypersensitivity reactions occurred within 24 hours in 8.2% of participants with the first dose and 3.9% with the second dose
- Anaphylaxis occurred in 4 (1.3%) of participants

ILI, influenza-like illness; IRR, infusion-related reaction; TEAE, treatment emergent adverse event; URTI, upper respiratory tract infection; UTI, urinary tract infection.
Invivyd Inc. Data on file.

ANAPHYLAXIS EVENTS
Cohort A

- **Defined using Sampson clinical criteria for diagnosing anaphylaxis[1]**
- **Two participants had anaphylaxis during the first infusion[2]**
  - These 2 events were classified as moderate (grade 2) hypersensitivity or infusion-related adverse reactions. The FDA reclassified these events as anaphylaxis adverse reactions.
  - Symptoms of these events included dyspnea, diaphoresis, erythema (face), chest discomfort, and tachycardia in 1 participant and flushing, dizziness, tinnitus, and wheezing in 1 participant
  - Treatment for both included oral diphenhydramine
- **Two participants had anaphylaxis during the second infusion[2]**
  - Both events were reported as potentially life threatening (grade 4)
  - Symptoms of these events included pruritus, urticaria, angioedema, dyspnea, and either erythema or flushing. One participant also experienced headache, dizziness, and chest pain; additionally, pruritus, erythema, and urticaria reoccurred in this participant within 24 hours of the initial onset of anaphylaxis
  - Both participants were treated with diphenhydramine and epinephrine, and 1 participant also received oral prednisone and metoprolol for an associated flare of an underlying condition
- **All 4 reactions led to permanent discontinuation of pemivibart[2]**

FDA, US Food and Drug Administration.
Invivyd. Fact Sheet for Healthcare Providers: Emergency Use Authorization for PEMGARDA.
1. Sampson HA, et al. *J Allergy Clin Immunol*. 2006;117:391-397. 2. Emergency Use Authorization for Pemivibart (PEMGARDA) Center for Drug Evaluation and Research (CDER) Review. https://www.fda.gov/media/177333/download?attachment. Action date March 22, 2024.

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SAFETY SUMMARY (THROUGH DAY 180)
Cohort B

- Adverse events occurred in 42.0% of pemivibart participants and 41.4% of placebo participants
- Most TEAEs were mild or moderate, and the most common TEAEs (≥3.0%) in pemivibart participants were URTI (8.2%), viral infection (7.3%), and ILI (5.4%), with similar percentages between pemivibart and placebo
- Study drug–related TEAEs occurred in 4.7% and 0% of pemivibart and placebo participants, respectively, with no study drug–related serious TEAEs or deaths
  - Study drug–related TEAEs leading to study drug dosing interruption occurred in 1.3% of pemivibart participants and to study drug discontinuation in 0.9% of pemivibart participants, with no interruptions or discontinuations in placebo participants
- Possible symptoms of infusion-related or hypersensitivity reactions occurred within 24 hours in 1.3% and 0.6% with the first dose and 2.5% and 0% with the second dose in pemivibart and placebo participants, respectively
  - No participants developed anaphylaxis

ILI, influenza-like illness; TEAE, treatment emergent adverse event; URTI, upper respiratory tract infection.
Invivyd Inc. Data on file.

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CONCLUSIONS

- This exploratory analysis of clinical endpoints through Day 180 following 2 doses of study drug administered 3 months apart showed:
  - An 84% relative risk reduction of RT-PCR–confirmed symptomatic COVID-19 in Cohort B (immunocompetent population) with pemivibart treatment vs placebo
  - A low rate of RT-PCR–confirmed symptomatic COVID-19 (3.7%) in pemivibart-treated participants in Cohort A (significantly immunocompromised population)
- In the CANOPY study, the protection provided by pemivibart was noted with contemporary variants and in a backdrop of contemporary immunity for participants
- Pemivibart was generally safe and well tolerated in most participants; anaphylaxis was observed in 0.6% (4/623) of participants treated with pemivibart in CANOPY

RT-PCR, reverse transcription polymerase chain reaction.

ACKNOWLEDGMENTS

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- This work was sponsored by Invivyd, Inc.

Questions

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