CLINICAL STUDY REPORT SYNOPSIS

Study Title:	An Interventional, Phase 1b, Randomized, Double-Blind, Sponsor-Open, Placebo-Controlled, Multi-Center, Dose-Finding Study to Evaluate Safety, Tolerability and Pharmacokinetics of Sisunatovir in Pediatric Participants up to Age 60 Months With Respiratory Syncytial Virus (RSV) Lower Respiratory Tract Infection (LRTI)
Study Number:	C5241009
Study Phase:	1b
Regulatory Agency or Public Disclosure Identifier Number:	NCT #: NCT06102174 EU CT #:2023-504425-39-00
Pediatric Investigational Plan Number:	PIP: EMEA-002529-PIP01-18
Study Intervention:	Sisunatovir (PF-07923568)
Study Sponsor:	Pfizer Inc. 66 Hudson Boulevard East New York, NY 10001
Study Initiation Date (first participant first visit [FPFV]):	15 February 2024
Primary Completion Date (PCD):	03 September 2024
Presentation of data in this CSR synopsis based on: **Study Completion (last participant last visit [LPLV]) Date:**	03 September 2024
Early Termination Status	On 28 August 2024, Pfizer made a business decision to terminate the ongoing sisunatovir adult and pediatric clinical studies. The decision was not due to any safety concerns. Participants already enrolled continued in the study and completed the last study visit.
CSR Version and Report Date:	**Document Version** / **Report Date** Final LPLV CSR Version 1.0 / 22 February 2025

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GOOD CLINICAL PRACTICE STATEMENT

This study was conducted in compliance with GCP guidelines and, where applicable, local country regulations relevant to the use of new therapeutic agents in the country/countries of conduct, including the archiving of essential documents.

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Number of Study Center(s) and Investigator(s):

A list of study centers and investigators involved in this study is provided in Appendix 16.1.4.1.

Publications:

None.

Brief Description of The Trial Design And Methodology:

This study was a randomized, double-blind, sponsor-open, placebo-controlled, multicenter study in RSV-infected outpatient and hospitalized neonates, infants, and children, 1 day up to 60 months of age with RSV-LRTI. This was a dose finding study to evaluate the pharmacokinetics (PK), safety, and tolerability of sisunatovir.

Three dosing cohorts were proposed for the study (Cohort 1, Cohort 2 and Cohort 3). Additionally, each cohort was further subdivided by age bands at the time of screening.

- Cohorts 1 and 2:

  A: >30 days to <6 months

  B: 6 months to <12 months

  C: 12 months up to 60 months

  D: 1 day to ≤30 days (ie, neonates and infants ≤30 days)
- Cohort 3:

  E: >30 days to <3 months

  F: 3 months to <6 months

  B: 6 months to <12 months

  D: 1 day to ≤30 days (ie, neonates and infants ≤30 days)

Although neonates are defined by the World Health Organization (WHO) as 0-27 days old, in this study the neonatal cohort refers to neonates and infants 1 day through 30 days old.

Sisunatovir or placebo were administered every 12 hours (q12h) in a 2:1 ratio, for a period of 5 consecutive days with a total of 10 doses for all cohorts. Sisunatovir doses expected to produce systemic steady-state exposures comparable to the 200 mg q12h adult dose were evaluated in dosing Cohort 1.

This report contains the results from all participants enrolled as of the decision to terminate the study.

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Number of Participants (planned and analyzed):

Table S1. Number of Participants (Planned and Analyzed)

Population	N	Definition
Planned	72	
Randomized	10	
FAS	10	All participants randomly assigned to study intervention and who took at least 1 dose of study intervention.
SAS	10	All participants randomly assigned to study intervention and who took at least 1 dose of study intervention. Participants were analyzed according to the product (sisunatovir / placebo) they actually received.
PK concentration set	6	All participants randomly assigned to study intervention and who took at least 1 dose of study intervention and in whom at least 1 concentration value could be reported.

FAS=full analysis set; SAS=safety analysis set

Diagnosis and Main Criteria for Inclusion and Exclusion:

This study enrolled pediatric participants (1 day to 60 months of age) with RSV-LRTI who had RSV related signs and/or symptoms present within 7 days of randomization. Premature infants (gestational age less than 35 weeks) and <1 year of post-natal age were excluded.

Study Intervention:

Sisunatovir formulation evaluated in this study was a dry powder blend. The matching placebo was formulated as a dry blend of mannitol and microcrystalline cellulose. The dry blends were filled into hydroxypropyl methylcellulose (hypromellose) capsules. Sisunatovir and placebo were administered orally or via nasogastric tube q12h for 5 days (2 doses daily Day 1-Day 5) /6 days (if not started with 2 doses on Day 1) for a total of 10 doses. Study intervention was administered to the participant by a parent, legal guardian or healthcare provider.

The manufacturing lot numbers for the study intervention(s) dispensed in this study are provided in Table S2.

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Table S2. Study Intervention(s) Administered

Study Intervention Description	Vendor Lot No.	Pfizer Lot No.	Strength/Potency	Dosage Form
Sodium Chloride Inhalation Solution 0.9% 15 mL vial	22F80	23-AE-00882	0 mg	Commercial vial / diluent
Sodium Chloride Inhalation Solution 0.9% 15 mL vial	23B54	23-AE-01009	0 mg	Commercial vial / diluent
PF-07923568 (Sisunatovir) 50 mg Blister strip 6 ct	PD21003	23-UU-00905	50 mg	Capsule
Placebo for PF-07923568 (Sisunatovir) 50 mg Blister strip 6 ct	PD21001	23-UU-00906	0 mg	Capsule
PF-07923568 (Sisunatovir) 50 mg Blister strip 6 ct	PD21002	23-UU-00904	50 mg	Capsule

Global Substantial Modifications

Table S3. Global Substantial Modifications

Date of Protocol Amendment	Amendment
11 Mar 2024	The primary purpose of this amendment was to address the new medication restrictions on acid reducing agents (eg, proton pump inhibitor, H_2 blockers and antacids) based on preliminary results from a drug-drug interaction study (C5241017), incorporate protocol clarifications and corrections to identified errors.
27 Jan 2024	The amendment addressed comments and feedback received from regulatory agencies, and incorporated protocol clarifications, updated inclusion and exclusion criteria based on the C5241015 study, and incorporated corrections to identified errors.
13 Sep 2023	The amendment addressed comments and feedback from regulatory agencies, and incorporated protocol clarifications, and corrections to identified errors.
26 Jun 2023	The protocol was amended to address comments received from the United States Food and Drug Administration, incorporated protocol clarifications, and corrected identified errors.

Global Interruptions and re-starts

Not Applicable.

Endpoints And Statistical Methods:

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Table S4. Objectives, Endpoints, and Statistical Methods

Objectives	Endpoints	Analysis Type	Analysis Population	Data Inclusion and Rules for Handling Intercurrent Events and Missing Data	Analysis Model
Primary					
• To evaluate the safety and tolerability of sisunatovir compared to placebo in participants with RSV-LRTI.	• Incidence of TEAEs.	• Safety	• Safety analysis set	• The sponsor data standard rules for imputation were applied.	• Descriptive statistics
	• Incidence of AEs and SAEs leading to discontinuations.	• Safety	• Safety analysis set	• The sponsor data standard rules for imputation were applied.	• Descriptive statistics
	• Incidence of clinically significant abnormal laboratory values and vital signs.	• Safety	• Safety analysis set	• The sponsor data standard rules for imputation were applied.	• Descriptive statistics
Secondary					
• To characterize the PK of sisunatovir in participants with RSV-LRTI.	• Plasma concentrations of sisunatovir at steady state (Day 3 or later).	• PK	• PK Concentration Population	• In all PK data presentations (except listings), concentrations BLOQ were set to zero. • In listings, BLOQ values was reported as "<LLOQ", where LLOQ was replaced with the value for the LLOQ. • For PK summary tables and plots of median profiles, statistics were calculated having set concentrations to missing if one of the following cases was true: • A concentration has been collected as ND (ie, not done) or NS (ie, no sample) • A deviation in sampling time was of sufficient concern or a concentration had been flagged anomalous by the pharmacokineticist/statistician.	• Descriptive statistics

AE = adverse event; BLOQ = below the lower limit of quantification; LLOQ = lower limit of quantification; PK = pharmacokinetics; SAE = serious adverse event; TEAE = treatment-emergent adverse event.

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SUMMARY OF RESULTS:

Participant Disposition

A total of 15 participants were screened for Cohort 1, and 5 (33%) of these were screen failures. All 10 enrolled participants were treated; 2, 3, and 5 participants were in Cohort 1A, 1B and 1C, respectively. All 10 participants completed treatment and follow-up.

Demographic and Other Baseline Characteristics:

Overall, the proportion of male and female participants was the same. Most of the participants were Asian (80%). The mean (standard deviation [SD]) age at screening was 14.06 (8.387) months. All participants tested positive for RSV (5 had RSV A and 5 had RSV B) with a mean (SD) RSV symptom duration of 3.9 (2.08) days at baseline.

Exposure:

All participants completed 5 days of treatment (10 doses).

Summary of PK/Safety Results

Table S5. Study C5241009 PK/Safety Results

Endpoints	Results
Primary:	
• Incidence of TEAEs. • Incidence of AEs and SAEs leading to discontinuations. • Incidence of clinically significant abnormal laboratory values and vital signs.	• A total of 17 AEs were reported in 7 participants (4 [66.7%] participants received sisunatovir and 3 [75.0%] participants received placebo). • All AEs were mild in severity. There were no SAEs or severe AEs. There were no AEs leading to dose modification, study intervention discontinuations or study discontinuations. Only 1 participant had a treatment-related AE (constipation), and this participant was in the placebo group. AEs were most commonly reported under the SOCs of Gastrointestinal disorders and Infections and infestations (both reported in 4 [40%] participants). The AEs that were reported in more than 1 participant were: diarrhea, vomiting, bronchitis, upper respiratory tract infection, and eczema, which occurred in 2 participants (20%) each. • Without regard to baseline abnormalities, all 10 participants had laboratory abnormalities during the study. None of the laboratory abnormalities were considered to be clinically significant and none were reported as AEs. No clinically meaningful findings in the vital signs measurements, or other observations related to safety were observed in this study.
Secondary:	
• Plasma concentrations of sisunatovir at steady state (Day 3 or later).	• Plasma PK samples were collected on study Day 3 and Day 5. Linear and semi-log median plasma sisunatovir concentration versus time following multiple oral BID dosing are provided in Figure S1.

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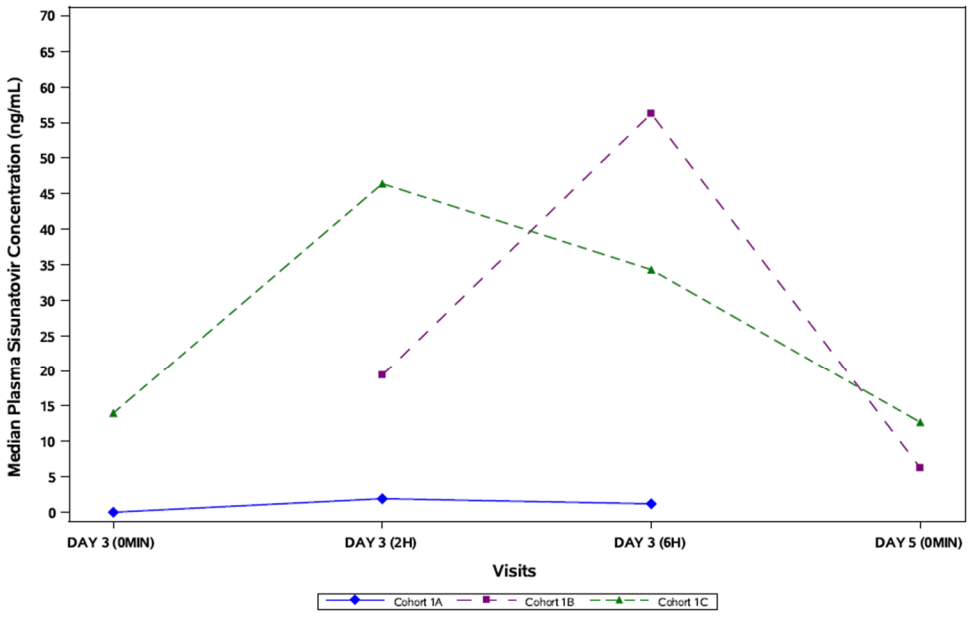
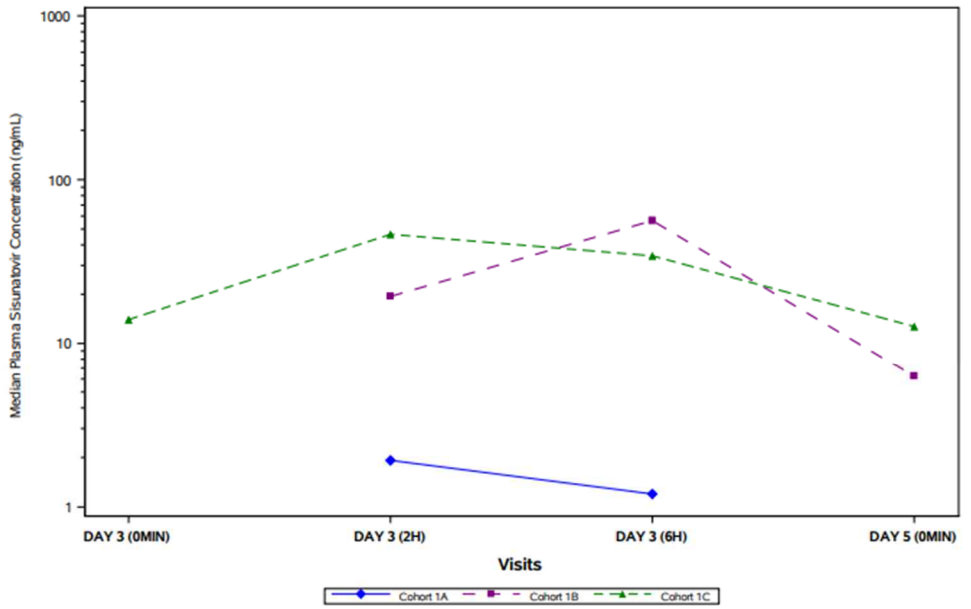
Figure S1. Median Plasma Sisunatovir Concentration – Time Plot – PK Concentration Set



Cohorts are divided into age bands: A: >30 days to <6m, B: 6m to <12m, C: 12m up to 60m
Summary statistics have been calculated by setting concentration values below the lower limit of quantification to zero.
The lower limit of quantification is 1.00 ng/mL.
PK concentration set includes participants presenting plasma/urine concentrations after administration of at least one dose of PF-07923568.
PFIZER CONFIDENTIAL SDTM Creation: 05NOV2024 (23:40) Source Data: adpc Table Generation: 02JAN2025 (23:34)
(Database snapshot date :15OCT2024) Output File: /nda_ph12/C5241009_CSR/adpc_f203



Cohorts are divided into age bands: A: >30 days to <6m, B: 6m to <12m, C: 12m up to 60m
Summary statistics have been calculated by setting concentration values below the lower limit of quantification to zero.
The lower limit of quantification is 1.00 ng/mL.
PK concentration set includes participants presenting plasma/urine concentrations after administration of at least one dose of PF-07923568.
PFIZER CONFIDENTIAL SDTM Creation: 05NOV2024 (23:40) Source Data: adpc Table Generation: 02JAN2025 (23:30)
(Database snapshot date :15OCT2024) Output File: /nda_ph12/C5241009_CSR/adpc_f204

Upper panel and lower panel are linear and semi-log scale, respectively.

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CONCLUSIONS:

Safety

Sisunatovir was safe and well tolerated in pediatric participants with RSV-LRTI. There were no deaths, severe AEs or SAEs. All TEAEs reported during the study were mild in severity.

PK

Because this study was terminated early with a small sample size (N=1 for Cohort 1A, N=2 for Cohort 1B, N=3 for Cohort 1C), the study was no longer powered to establish the PK of sisunatovir in pediatric participants with RSV-LRTI.