SUMMARY REPORT

Study Title:	PRISM: An Open-label, Multi-Center Extension Study to Investigate the Efficacy and Safety of Cobomarsen (MRG-106) Following Systemic Treatment in Subjects with Cutaneous T-Cell Lymphoma (CTCL), Mycosis Fungoides (MF) Subtype, Who Have Completed the SOLAR Study
Product Name or Number:	Cobomarsen (MRG-106)
Protocol Number:	MRG106-11-203
EudraCT Number:	2018-003748-22
Developmental Phase:	2 (Extension Study)
Indication Studied:	Cutaneous T-Cell Lymphoma, Mycosis Fungoides Subtype
First Subject, First Visit	01 October 2019
Last Subject, Last Visit:	27 July 2020
Data Cutoff	27 July 2020
Study Sponsor:	miRagen Therapeutics, Inc. 6200 Lookout Road Boulder, CO 80301 USA
Sponsor's Responsible Medical Officer:	Diana M. Escolar, MD, FAAN
Date of Report:	22 July 2021

Quality Assurance Statement

This trial was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and clinical research guidelines established by the Code of Federal Regulations (Title 21, CFR Parts 50, 56, and 312) and International Conference on Harmonization (ICH) Guidelines.

TABLE OF CONTENTS

LIST OF TABLES

ABBREVIATIONS AND DEFINITIONS OF TERMS

Abbreviation/Specialist Term	Definition
AE	Adverse event
CR	Complete response
CTCAE	Common Terminology Criteria for Adverse Events
CTCL	Cutaneous T-cell lymphoma
ECG	Electrocardiogram
MedDRA	Medical Dictionary for Regulatory Activities
MF	Mycosis fungoides
MRG-106	Cobomarsen
mSWAT	Modified Severity Weighted Assessment Tool
NCI CTCAE	National Cancer Institute Common Terminology Criteria for Adverse Events
PD	Progressive disease
PDu	Unconfirmed progressive disease
PR	Partial response
SAE	Serious adverse event
SD	Stable disease
SOLARx	Crossover arm of SOLAR clinical trial

1. INTRODUCTION

This open-label study (MRG106-11-203, PRISM) was an extension of the investigational study (MRG106-11-201, SOLAR), which compared the safety and efficacy of cobomarsen (the investigational product) and vorinostat (the active comparator) in subjects with cutaneous T-cell lymphoma (CTCL), mycosis fungoides (MF) subtype. The primary objective of the PRISM study was to evaluate the efficacy of cobomarsen in subjects with MF who had confirmed disease progression following treatment with vorinostat in the SOLAR study.

The PRISM study was terminated early once a crossover arm was added to the SOLAR trial, allowing for subjects still receiving active treatment when PRISM closed to transfer to the SOLAR crossover arm (SOLARx) to continue cobomarsen treatment.

2. STUDY OBJECTIVES

The primary objective of the PRISM study was to evaluate the efficacy of cobomarsen in subjects with MF who had confirmed disease progression following treatment with vorinostat in the SOLAR study.

A secondary objective was to investigate the safety and tolerability of cobomarsen in subjects with MF. An additional exploratory objective was to characterize the pharmacodynamic effects of cobomarsen in subjects with MF who had been previously treated with vorinostat.

As a result of the early termination of the PRISM study, none of the study's objectives were completed as planned.

3. METHODOLOGY

Cobomarsen was administered by intravenous 2-hour infusion at a dose of 282 mg of the active moiety (equivalent to 300 mg of the active pharmaceutical ingredient or sodium salt form) on Days 1, 3, 5, 8, and weekly thereafter. Subjects were to remain on study treatment until disease progression or other protocol-defined treatment discontinuation criteria were met.

Efficacy was to be assessed using composite global response criteria, including radiological imaging, flow cytometry, and assessment of skin disease (using the modified Severity Weighted Assessment Tool [mSWAT]). Response was to be assessed as complete response (CR), partial response (PR), stable disease (SD), unconfirmed progressive disease (PDu), or progressive disease (PD). Disease progression in any compartment was to be confirmed by repeated measurement 28 days (±3 days) after the first determination of progression.

Safety assessments included adverse events (AEs), clinical laboratory evaluations, electrocardiograms (ECG), vital signs, and physical examination. AEs were coded by preferred

term and system organ class using the Medical Dictionary for Regulatory Activities (MedDRA), version 21.0. Severity was assessed using the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE), version 5.0. Relationship to study treatment was based on investigator's attribution.

4. NUMBER OF SUBJECTS (PLANNED AND ANALYZED)

Up to 60 subjects were expected to be enrolled. A total of 8 subjects had been enrolled when the trial was terminated in July 2020.

5. RESULTS

Note: As this study was terminated early, the subject data were not completely monitored prior to database lock.

Eight subjects (5 males and 3 females) were enrolled at 7 clinical sites (3 subjects in France, 2 in Belgium, and 3 in the United States). The average age of subjects at screening (± standard deviation) was 61.1 (± 15.3) years. The race/ethnicity of enrolled subjects was white/not Hispanic or Latino (4 subjects); Black/not Hispanic or Latino (1 subject); and Not Reported (3 subjects).

Table 1 provides a summary of the disposition, cobomarsen exposure, and response data for all enrolled subjects.

Upon early termination of the study, 5 of the 8 subjects rolled over to the crossover arm of the SOLAR study to continue cobomarsen treatment (as noted in Table 1). Best response to cobomarsen was reported as SD for 6 of 8 subjects, PR for one subject, and PD for one subject. One subject ended treatment because of physician's decision (lack of benefit), one due to PD, and one because of an AE.

Table 1. Summary of Cobomarsen Exposure, Best Response to Treatment and Disposition of All Enrolled Subjects

Subject	MF Stage at Baseline	Duration of Cobomarsen Exposure (Days)	Best Response to Therapy[1]	Ended Treatment?	Primary Reason for End of Treatment
1	1B	49	SD	Yes	Physician's decision/lack of benefit
2	1B	105	SD	Yes	Subject rolled over to SOLARx
3	1B	113	PR	Yes	Subject rolled over to SOLARx
4	Not reported	149	SD	Yes	Subject rolled over to SOLARx
5	1B	114	SD	Yes	Subject rolled over to SOLARx
6	IIB	44	PD	Yes	PD
7	IIB	104	SD	Yes	Subject rolled over to SOLARx
8	IIB	71	SD	Yes	Adverse event

MF = mycosis fungoides; PD = progressive disease; PR = partial response; SD = stable disease; SOLARx = crossover arm of SOLAR clinical trial (EudraCT 2018-000727-13)

[1] Skin response based on mSWAT

There were no deaths in the study. Six of the 8 subjects had AEs reported, 3 of which were serious adverse events (SAE): Grade 3 catheter site infection resulting in dosing interruption; Grade 3 carotid artery stenosis (in a subject who had a history of carotid artery disease); and Grade 3 sepsis (secondary to acute pyelonephritis caused by *Klebsiella pneumoniae* complicated by bacteremia in a subject with multiple urinary tract infections). This subject had multiple Grade 3 AEs, which resulted in dosing interruptions, before treatment was discontinued because of the SAE of sepsis.

In most cases, AEs were Grade 1 or 2, considered unrelated to treatment, and did not cause any change in dosing. A summary of the non-serious AEs is provided in Table 2.

Table 2. Summary of Non-Serious Adverse Events by Severity and Overall

	Number of Events by Severity				Total
System Organ Class ***Preferred Term***	**Grade 1 (n=17)**	**Grade 2 (n=14)**	**Grade 3 (n=9)**	**Grade 4 (n=0)**	**(N=40)**
Gastrointestinal disorders					**1**
Anal fissure	1				1
General disorders and administration site conditions					**10**
Fatigue	2	1			3
Asthenia		2			2
Pyrexia	1		1		2
Feeling hot		1			1
Oedema peripheral	1		1		2
Skin and subcutaneous tissue disorders					**8**
Pruritus	3	1			4
Pain of skin		1			1
Skin erosion		1			1
Skin ulcer		1			1
Dermatitis acneiform	1				1
Infections and infestations					**2**
Pyelonephritis acute			1		1
Klebsiella infection			1		1
Respiratory, thoracic and mediastinal disorders					**1**
Lung disorder	1				1
Musculoskeletal and connective tissue disorders					**5**
Myalgia		2			2
Musculoskeletal pain	1				1
Limb discomfort		1			1
Pain in extremity		1			1
Nervous system disorder					**2**
Headache		1	1		2
Metabolism and nutrition disorders					**3**
Hyperuricaemia	1				1
Hyperglycaemia	1				1
Hypokalaemia			1		1
Vascular disorders					**3**
Hypertension		1	2		3
Cardiac disorders					**1**
Atrial fibrillation			1		1
Investigations					**3**
Gamma-glutamyltransferase increased	1				1
Haemoglobin decreased	1				1
Oxygen saturation decreased			1		1
Psychiatric disorders					**1**
Insomnia	1				1

6. CONCLUSIONS

Among the 8 subjects who participated in the PRISM clinical trial, the best response to treatment with cobomarsen was SD for 6 subjects, PD for one subject, and PR for one subject.

There was one discontinuation due to an AE (SAE of sepsis).

There were no deaths in the study. Three subjects had one SAE each, all of which resolved.

7. SPONSOR'S APPROVAL

Study Title: PRISM: An Open-label, Multi-Center Extension Study to Investigate the Efficacy and Safety of Cobomarsen (MRG-106) Following Systemic Treatment in Subjects with Cutaneous T-Cell Lymphoma (CTCL), Mycosis Fungoides (MF) Subtype, Who Have Completed the SOLAR Study

Protocol Number: MRG106-11-203

Date of Report: 22 July 2021

I have read this summary report and confirm that to the best of my knowledge it accurately describes the conduct and results of the study.

Judy Ruckman

I am approving this document.

Judy Ruckman 07/22/2021 01:10 PM EDT

Judy Ruckman, Ph.D.
Sr. Director, Regulatory Affairs
Viridian Therapeutics, Inc.
(formerly miRagen Therapeutics, Inc.)

Date