Protocol of a Phase II MATIK Trial

1. Introduction and Background

MATIK is a newly discovered, highly contagious viral skin disease that causes serious skin rash and infections in patients, and could even be life threatening. Several scientific labs and drug companies are actively engaged in developing drugs to battle the emerging epidemic. From all the biological and animal studies, three medications, one oral Pill and two skin gels, appeared to be promising. We denote the three medications by Pill A, Gel B and Gel C. Phase I trials have already been conducted to determine their maximum tolerated doses among patients.

Due to urgent need, researchers/clinicians decide to conduct a phase II trial to evaluate the safety and adherence of all the three medications simultaneously. Based on the information collected from the Phase I trials, and earlier cell line and animal studies. The following doses will be used in the trial.

Table 1 Recommended doses/administration schedule

Pill A	200 mg, once a day for 4 weeks
Gel B	1% gel concentration; three times a day on affected areas, daily use for 4 weeks
Gel C	2% gel concentration; once a day on affected areas, daily use for 4 weeks.

2. Study Design

This is a Phase 2, multi-site, randomized, open-label, three-arm crossover study.

2.1 Patient population and recruitment

Approximately 180 MATIK patients will be recruited from a variety of health care facilities, including hospitals, primary care clinics, and community-based health services. Recruitment materials will be approved by site Institutional Review Boards/Ethics Committees (IRBs/ECs). Accrual is expected to be completed in approximately 6-9 months per site.

2.2 Study Regimen

Study participants will be randomized to one of six regimen sequences (Sequence 1-6, see Table 2). Each sequence will consist of three 4 week periods of study product administration followed by at least a one-week washout period. The duration of product administration including the two washout periods is approximately 15 weeks. Participants will receive study products at the recommended dose, and be administered in the order designated by their randomized sequence (1-6).

Table 2: Study Regimen

Sequence	Period 1 (4 weeks)	Washout (~1 week)	Period 2 (4 weeks)	Washout (~1 week)	Period 3 (4 weeks)	Follow-up (~1 Week)
1	Pill A		Gel B		Gel C	
2	Gel C		Pill A		Gel B	
3	Gel B		Gel C		Pill A	
4	Gel B		Pill A		Gel C	
5	Pill A		Gel C		Gel B	
6	Gel C		Gel B		Pill A	

3. Study Objectives and Endpoints

3.1 Primary Objectives

Since MATIK is a chronic condition, patients will reply on long-term medications to control their viral loads. The primary objective of this trial is to compare the safety and adherence profiles of Pill A, Gel B, and Gel C, i.e. 1) whether the medications are safe for patients, 2) and whether patients could easily adhere to medication schedules so that long term use is feasible.

3.1 Secondary Objectives

The secondary objective of the trial is to have preliminary assessment and comparison of systemic and local Pharmacokinetics (PK) of Pill A, Gel B, and Gel C. Additionally, the investigators are interested to: 1) assess the correlation of PK with adherence measures and the occurrence of adverse events and 2) identify

demographic factors associated with product adherence and whether they differ by product used (Pill or gel) or regimen (three times a day or once a day).

3.3 Endpoints and their collection schedules

Primary endpoints:

During each week of the 4-week trial periods, participants were followed up every week to record the following measures:

- **Safety:** The number of grade 2 or higher adverse events occurred during that week.
- **Adherence:** The number of days (out of 7 days) that patients are able to take pills or apply gels as prescribed.

Secondary endpoints:

- **Pharmacokinetics**: The viral loads in the blood plasma and affected skin tissues were measured at the beginning and at the end of each period.

Demographics:

- Demographic data including age, gender and race of the recruited patients were collected at baseline.

The collected data were saved in two .cvs files. Baseline demographics and viral loads before and after each treatment periods were saved in *baseline.csv,* safety and adherence endpoints were saved in *endpoints.csv.* Their code books were saved in *Dictionary.xlsx.*

Please analyze the data to address the primary and secondary scientific questions, and write a report accordingly.

In your report, please also include a discussion on next step Phase III trial. For example, based on your analysis results, which treatment(s) you would recommend for Phase III trial ? Which study design you would like to use? What information in the Phase II trial could help you plan for the next step Phase III trial? What additional inform you would need?

Note: Although data were collected from various places, for the purpose of this analysis, we assume there are NO site specific differences.