STUDY SYNOPSIS (continued)

Name of sponsor company: Verrica Pharmaceuticals, Inc.

Name of finished product: VP-102 (0.7% w/v cantharidin)

Name(s) of active ingredient(s): Cantharidin

application. Assessments will be recorded by a research team member on the ERT form. ERT visits may not be conducted by a blinded assessor. Phone assessments will not be conducted if there is no treatment administered. The ERT includes questions related to removal of study drug and records the intensity of any local skin reactions, adverse events and concomitant medications (ConMeds). The subject and/or guardians will have time to ask questions and review any concerns. Concerns and events will be assessed and in the event any adverse events present a safety concern, an unscheduled clinic visit will be scheduled.

Each subject will be evaluated and treated as follows:

- Screening Period (Up to 14 days prior to first treatment).

- Safety Evaluation Period (Treatment Visit 1)
  - Confirm that subject still meets criteria (Dermatologic exam/lesion count; ability to attend study visits).
  - Lesion count and CDLQI assessment.
  - Study drug application.
  - Removal of Study drug 24 hours after application.
  - 24-hour, in-office ERT, within 48 hours (+/- 1 day) after treatment.
  - ERT phone calls at Days 7 and 14 after treatment.

- Safety and Efficacy Evaluation Period (visits targeted 21 days after prior visit)
  - Treatment Visit 2: Lesion count by blinded assessor, dermatologic exam, CDLQI assessment, ERT, and Study drug application (if subject has treatable lesions remaining). Removal of Study drug 24 hours after application. ERT phone calls at 24 hours and Days 7 and 14 after treatment (if treated).
  - Treatment Visit 3: Lesion count by blinded assessor, dermatologic exam, CDLQI assessment, ERT, and Study drug application (if subject has treatable lesions remaining). Removal of Study drug 24 hours after application. ERT phone calls at 24 hours and Days 7 and 14 after treatment (if treated).
  - Treatment Visit 4: Lesion count by blinded assessor, dermatologic exam, CDLQI assessment, ERT, and Study drug application (if subject has treatable lesions remaining). Removal of Study drug 24 hours after application. ERT phone calls at 24 hours and Days 7 and 14 after treatment (if treated).

- End of Study (targeted 21 days after Treatment Visit 4)
  - Lesion count by blinded assessor, dermatologic exam, CDLQI and ERT.

Study Duration: The study duration from Treatment Visit 1 through the end of study is approximately 84 days (12 weeks).

Subject Participation: Pre-study screening for eligibility (informed consent and assent, [assent when applicable], demographics, physical exam, prior and concomitant medications and molluscum and

a. Screening can occur up to 14 days prior to Study drug application on Day 1. Screening can occur on the same day as treatment Day 1/Study drug application. An IRB-approved ICF/Assent must be signed before any study specific procedures are performed.
b. Out of Window Parameters: Subjects may be scheduled 21+/- 4 days after treatment in the event of scheduling conflict. If possible, the next treatment visit should be scheduled 21 days after the last treatment. The 24-hour onsite visit may be conducted within 48 hours of Treatment 1. The 24 hour phone contact may be conducted at +/- 4 hours. The Day 7 and Day 14 phone contact may be conducted at +/- 24 hours. If it is found during any treatment visit that all treatable molluscum lesions are cleared, the investigator will only conduct safety and ERT assessments and will not apply additional treatment.
c.. Subjects who clear all lesions at study visits prior to Day 84 will return to the office for each treatment visit (even if no treatment is applied) to complete all study related assessments. A final safety assessment and study completion form will be completed at the Day 84 (EOS) visit.
d. Demographics: date of birth, sex, race/ethnicity will be collected.
e. Vital signs (e.g., temperature & heart rate) will be obtained at each treatment prior to application of Study drug.
f. Limited physical examination. Symptom or AE-directed physical examination may be performed if warranted. (See Source/CRF for a more detailed description)
g. Regional lesion counts (head/neck, chest/abdomen, back/buttocks, groin, upper/lower extremities) should be performed. Lesion counts completed at Treatment Visits 2, 3, 4 and EOS should be performed prior to the dermatologic exam and ERT assessments and will be obtained by a blinded assessor. The blinded assessor does not have to be the same person at each visit.
h. Unscheduled visits may be completed when clinically warranted (e.g. if a subject reports signs or symptoms classified as a treatment emergent AE and requires further evaluation)
i. CDLQI assessment to be completed by the subject or guardian prior to Study drug application and each treatment visit regardless whether treatment was administered.
j. To be performed prior to Study drug application and at EOS in any females of childbearing potential (females that are capable of menstruating).
k. Photographs of molluscum lesions will be obtained by the research team at selected clinical sites only for every visit for every randomized subject. Photos of the 3 most severe areas will be obtained. If there are no lesions remaining, the same areas will be photographed until EOS regardless of whether lesions are present.
l. Study drug may be gently removed from individual lesions prior to 24 hours of application in the event of significant blistering, significant pain or treatment emergent AEs. Study drug should not be removed from the remaining unproblematic lesions until the 24-hour time point is reached.
m. An Evaluation of Response to Treatment (ERT) in-person 24-hour assessment will be conducted within 48 hours (+/- 1 day) after the initial treatment application and after Study drug has been removed. Phone assessments will be conducted at 7 and 14 Days after Treatment Visit 1. Phone assessments will be conducted at 24 hours, 7 Days and 14 Days after Treatment Visits 2, 3 and 4. Phone assessments will not be conducted for those subjects that did not receive treatment on their last visit. Assessments will be recorded by the research team member on the Evaluation of Response to Treatment (ERT) form. All ERT safety assessments must be conducted by a qualified member of the research team who is not utilized as a blinded assessor during the subject's study participation. The blinded assessor may be utilized for a subject's initial screening and enrollment but no additional study related activities other than lesion counts. The blinded assessor does not have to be the same person at each visit.
n. Subjects will be given take-home instructions describing the possible local skin reactions and what to expect over the next 24 hours to several months. A 24-hour emergency number will also be provided. The next visit date/calls and time will be indicated on the form. A Local Skin Reaction Guide for subjects will be reviewed at the clinic with the subject /guardian by the research team with copies provided for home use in the required follow-up phone calls. Both take home instructions and LSR Guide will be provided and reviewed after each treatment to ensure understanding and confirm the education materials are available.

1.0 INTRODUCTION

1.1 MOLLUSCUM CONTAGIOSUM

The causative agent of molluscum contagiosum (molluscum) is the molluscum virus, a dermatotropic DNA poxvirus. Molluscum is common in the pediatric population and is prevalent worldwide. It produces small flesh-colored papules and papulovesicles, 1-4 mm in diameter, which typically have an umbilicated or dimpled center. There is often little inflammation associated with molluscum papules, and the presence of an inflammatory reaction to such papules often heralds resolution of the disease. Molluscum lesions are generally not painful, but they may itch or become irritated. Picking or scratching the bumps can lead to autoinoculation, secondary bacterial infection or scarring.

Molluscum is spread readily by autoinoculation and by person-to-person contact. The virus may also be transmitted by touching objects such as towels, clothing, or toys. Most immunocompetent individuals will spontaneously clear the disease in an average of 13 months, although 25% children still have the disease after 18 months.[3] Spread to siblings and friends, as well as the development of additional lesions in neighboring sites during this time causes parental angst, socialization challenges for the afflicted individuals[1, 2] and has been shown to negatively impact quality of life.[3] The highest incidence is in children up to 14 years of age, where the incidence rate ranges from 12 to 14 episodes per 1,000 children per year.[4]

There is no approved product by the Food and Drug Administration (FDA) for the treatment of molluscum. Given that there are no approved options, physicians employ a variety of treatment approaches including (a) benign neglect; (b) curettage; (c) cryotherapy; (d) expressing the molluscum bodies; (e) retinoic acid creams; (f) caustic agents; (g) topical immunotherapeutics; and (h) non-standardized, compounded cantharidin products of various purity, formulations, and strengths.

1.2 CANTHARIDIN

Cantharidin (1,2-dimethyl-3,6-epoxyperhydrophthalic anhydride) is a lipophilic natural compound that can be isolated from the body fluids of the blister beetle, primarily of the family Meloidae. Blister beetles are found in many parts of the world, including the southern United States and Asia (*Mylabris Cichorii L* and *Mylabris*

2. Separate assessments for clearance will be repeated for both Visit 3 and Visit 4.

2.0 STUDY DESIGN

2.1 BASIC DESIGN CHARACTERISTICS

This is a Phase 3, multi-center, randomized, double-blind, placebo (vehicle)-controlled, pivotal study that will be conducted in the United States to determine the efficacy and safety of VP-102 following treatment of molluscum lesions for up to 4 treatments, every 21 days, with VP-102/placebo in 250 pediatric subjects (2 years or older). Subjects will receive active 0.7% cantharidin VP-102 or placebo in a 3:2 ratio. Duration of molluscum lesions prior to Treatment Visit 1 will be recorded but will not be an inclusion/exclusion requirement.

Study drug (VP-102 or placebo) will be supplied in single-use applicators, with one applicator sufficient to treat up to approximately 50 molluscum lesions. If required, due to the number and size of lesions, a second single-use applicator may be used per subject. No more than 2 applicators will be permitted per subject per treatment. The film-forming Study drug solution will be applied and left on the lesions for 24 hours before the subject/guardian washes the lesions with soap and warm water. Study drug may be removed prior to the 24-hour time point in the event significant blistering, significant pain or treatment-emergent AEs are experienced.

Molluscum lesions will be treated without occlusion in all anatomic areas including the face, trunk, back, arms, legs, hands, feet, anogenital region and buttocks. For study enrollment, the physician must be willing to treat all lesions initially present. Lesions that develop during the course of the study within 10mm of the eyelid margins or the margin of any mucosal surface should be evaluated carefully to ensure that they can be safely treated. Non-mucosal genital area lesions and inflamed lesions are considered treatable.

The study duration from Treatment Visit 1 through the Day 84 (EOS) visit is approximately 84 days (12 weeks). Pre-study screening for eligibility (informed consent, and assent (if assent is applicable), demographics, physical exam, prior and concomitant medications and molluscum and medical history) will occur up to 14 days before, or on Treatment Visit 1. Subjects who do not meet the inclusion criteria at Treatment Visit 1 will be discontinued and treated per standard of care. Those subjects

that continue to meet criteria will be randomized per IWRS and treated with application of VP-102 or placebo solution to all molluscum lesions every 21 days (± 4 days) for a maximum of 4 treatment sessions. Subjects who completely clear all treatable lesions prior to Day 84 will complete the remainder of the Treatment Visits in order to monitor safety. If new lesions appear on a previously cleared subject, they should be treated. In the event of scheduling conflicts in subsequent visits after the first treatment, subjects may be scheduled on 21 ± 4 days following their previous treatment. The next study visit should then be scheduled 21 days after the previous treatment. In the event a subject misses a treatment visit and is outside the 4-day study window, they may return and be treated at the next available opportunity with the subsequent treatment visit scheduled 21 days later to facilitate up to 4 treatments within 84 Days.

The final study visit assessment must be completed on or before Day 100. Should it become clear that the subject would be unable to complete the EOS on or before Day 100, the subject should be brought in for their EOS visit on or before Day 100, regardless of the number of days since their last Treatment Visit (eg., a missed treatment may cause the subject to fall outside this window of 16 days).

Subjects who are unable to attend the in-office EOS visit may have the option of an EOS home visit by a qualified member of the research team if this is within the site's standard of practice. Consent for Home Visit will be included in the initial consent process. Subjects who continue to require treatment outside the specified study windows must be treated allowing for EOS to occur before or on Day 100. Subjects who are not assessed as 100% cleared of all treatable lesions at the EOS visit will have completed the study and will be further treated per standard of care at their physician's discretion but may not be re-enrolled in this study.

Evaluation of Response to Treatment (ERT) will be performed by the investigator or trained member of the research team, who is not a blinded assessor for that subject, at each treatment visit. An additional 24-hour in-office assessment will be conducted within 48 hours (+1 day) after the first treatment and at the EOS visit. Qualified study personnel who are not blinded assessors for the subject, will conduct ERT phone calls at 7 and 14 days after Treatment Visits 1. In addition, ERT phone calls at 24-hours as well as 7 and 14 days after Treatment Visits 2, 3 and 4 will be performed to assess treatment response, document any local skin reactions and any medical interventions taken if treatment was administered. The following clinical responses will be recorded

- Proportion of subjects exhibiting complete clearance of all treatable molluscum lesions (baseline and new) on the Day 42 visit.

- Proportion of subjects exhibiting complete clearance of all treatable molluscum lesions (baseline and new) on the Day 21 visit.

Exploratory endpoints:

- Change from baseline of the composite score from the Children's Dermatology Life Quality Index (CDLQI) assessment at the EOS visit to measure the quality of life and impact of skin disease in the subset of subjects 4-16 years of age.

- Percent reduction of all treatable molluscum lesions (baseline and new) from baseline at the EOS visit.

- Change from baseline in the number of treatable molluscum lesions (baseline and new) at the EOS visit.

- Proportion of subjects exhibiting a 75% or greater reduction of all treatable molluscum lesions (baseline and new) at the EOS visit.

- Proportion of subjects exhibiting a 90% or greater reduction of all treatable molluscum lesions (baseline and new) at the EOS visit.

- Subject reported spread to household members as measured by any new occurrence of molluscum in household members of subject.

2.3.1 Safety

The following safety parameters will be assessed:

- Limited physical examinations will be performed by a qualified medical practitioner at screening and at EOS visits. Height and weight will be recorded at the screening visit and at the EOS visit. Unscheduled physical examinations will be performed when clinically warranted (e.g., if a subject reports signs or symptoms requiring further evaluation).

- Vital signs (e.g., heart rate and temperature) will be obtained at all treatment visits prior to treatment. A final assessment of vital signs will be obtained at the EOS visit.

4. Provide subjects/guardians with both verbal and the written take-home instructions on potential side effects and complications, contact information of the study investigator/study coordinator for questions or concerns, and a copy of their signed informed consent (Screening Day and/or Day 1 only). Subjects will be provided a LSR guide to assist the Site in collecting the required ERT information related to the treated areas.

5. Subjects should wash clothing, bedding and towels on a regular basis with hot water to minimize re-inoculation. Subjects are encouraged to wash their hands regularly with soap and water and discouraged from scratching lesions, which can spread disease.

3.3 STORAGE AND HANDLING OF INVESTIGATIONAL PRODUCT

Study medication is packaged in subject-specific kits within cardboard boxes that contain 5 individually packaged applicators. Each applicator is individually contained in a labeled zip-top bag. The zip-top should not be opened until treatment is ready to be applied.

The applicator is labeled with the Investigational New Drug (IND) application number and an applicator/kit number, which will be assigned to a specific subject. The label also indicates the date of manufacture and "Caution: New Drug--Limited by Federal Law to Investigational Use" and "Warning: Flammable Liquid." The applicator warnings indicate characteristics of the Study drug including the required labeling "Warning: Flammable Liquid" and the yellow toxic chemical symbol with the phrase "Warning: Highly Toxic". Used applicators are not to be discarded after use but should be returned to their zip-top bags and stored in the subject-specific carton until the study monitor completes accountability at the monitoring visit. All used and unused study medication is to be discarded at the site in a sharps container, or per the site's SOP for disposal, after the study monitor has reviewed and confirmed accurate accountability. Those sites that are not allowed to dispose of the Study drug at their site will make arrangements with the Sponsor for return and destruction.

Study drug must be stored at controlled room temperature (68°-77°F; excursions of 59°-86°F are acceptable for short periods) in a secure, dry location with limited and controlled access, and out of direct light. Extended exposure to extreme temperature conditions or to direct light should be avoided (e.g. Study drug left in an unoccupied

remaining). Removal of study drug 24 hours after application. ERT phone calls at 24 hours and Days 7 and 14 after treatment.

4. End of Study: (targeted 21 days after Treatment Visit 4)

- Lesion count by blinded assessor, dermatologic exam, CDLQI and ERT assessments.

The Screening period permits screening up to 14 days prior to Treatment Visit 1. An IRB-approved Informed Consent and Assent (assent when applicable) will be signed before any study specific procedures are performed. The Safety Evaluation Period (Treatment Visit 1) will begin with confirmation that the subject still meets study criteria (e.g., Dermatologic exam/lesion count; ability to attend study visits). After the screening/enrollment study activities have been completed, all safety assessments must be completed by a qualified member of the research team who is not utilized as a blinded assessor for an individual subject's efficacy assessments. Lesion counts will be performed at each treatment visit by a blinded assessor prior to each treatment application. It is not required that the blinded assessor be the same person for each study visit.

Subject impact on quality of life will be assessed using the CDLQI during each treatment visit, prior to the application of Study drug. ERT in-person safety assessments will be conducted during the initial treatment visit and within 48 hours after the initial treatment application (and must be after Study drug has been removed). Subsequent safety follow-ups will include ERT phone assessments at 24 hours, 7 and 14 days after each treatment. ERT will also be assessed at each 21-day in person visit prior to Study drug application. During the Safety and Efficacy Evaluation Period, subjects will be scheduled every 21 days (+/- 4 days); in the event that there are scheduling conflicts preventing a 21-day return visit, the next treatment will be scheduled at 21 days after the last treatment. In the event a subject misses a treatment visit and is outside the study window, they may return and be treated at the next available opportunity with the subsequent visit scheduled 21 days after treatment to facilitate up to 4 treatments within 84 Days. The final study visit assessment must be completed on or before Day 100. Subjects who are not assessed as 100% cleared of all treatable lesions at the EOS visit will have completed the study and will be further treated per standard of care at their physician's discretion. AEs will be assessed at every study visit.

4.2.2 Safety Evaluation Period (Treatment Visit 1)

Screening and Treatment Visit 1 may occur on the same day. The following evaluations will be performed and recorded in the electronic case report form (eCRF):

1. Confirmation that the inclusion/exclusion criteria are met.
2. Dermatologic exam:
    a. Regional molluscum lesion count (head/neck, chest/abdomen, back/buttocks, groin, and upper/lower extremities) including treated and untreated lesions.
    b. Presence of any confounding dermatologic diseases such as atopic dermatitis.
3. Medical history to assess any changes since screening (as described in Section 4.2.1).
4. Review and recording of any concomitant medications and non-pharmacologic treatments or procedures in the last 14 Days prior to enrollment and since the last study visit.
5. The presence of household members with molluscum. If these household members are enrolled in the study and if so the household member's subject ID number.
6. Vital signs (heart rate and temperature).
7. Limited physical examination.
8. CDLQI assessment.
9. Urine pregnancy test for females of child-bearing potential, defined as capable of menstruating, to determine protocol eligibility.
10. ERT assessment (LSRs, AEs, ConMeds)-prior to treatment.
11. Photographs taken before application of the Study drug (at selected sites only).
12. Application of Study drug.

13. Subjects will be given take-home instructions describing potential local skin reactions and what they might expect throughout the course of the study, as well as recommendations for wound care, when it is important to call their doctor and instructions for who to contact in an emergency.

14. A local skin reaction guide for subjects with specific photos identifying the various skin reactions and examples of intensity will be reviewed at the clinic with the subject/guardian by the research team. Should a subject report experiencing excessive blistering or another adverse event needing physician assessment, they will be scheduled for an unplanned study visit and safety evaluation at the next available opportunity.

15. Review and record any AEs and concomitant medications.

16. Depending on age of subject, subject or parent/guardian will wash off the Study drug with warm water at 24 hours after application of Study drug. Subjects/guardians may gently remove the Study drug from lesions without the use of a washcloth in problematic areas prior to the directed 24 hours if the lesions have already blistered or if the subject is experiencing significant pain. Study drug should not be removed from the additional lesions, where possible, unless significant blistering occurs or the 24-hour time point is reached, whichever comes first.

17. A 24-hour in-person follow-up visit will be conducted within 48 hours (+/- 1 day) following the initial treatment. Study drug must have been removed before the actual visit. Additional ERT assessments will be conducted over the phone at 7 and 14 days after treatment.

4.2.3 Safety and Efficacy Evaluation Period: (Treatment Visits 2, 3 and 4)

1. Review and recording of any concomitant medications and non-pharmacologic treatments/procedures since previous visit.

2. Review and recording of any AEs (before and after Study drug application).

3. Vital signs (heart rate and temperature) before Study drug application.

4. Dermatologic exam (as described in Section 4.2.1) with counting of molluscum lesions. Lesion counts must be conducted and documented by a blinded assessor who is not familiar with the subject's safety assessments or response to treatment.

5. CDLQI assessment.

6. ERT assessment (LSRs, AEs, ConMeds)-prior to treatment. (May not be conducted by a research team member who is utilized as the subject's blinded assessor)

7. Urine pregnancy test for females of child-bearing potential to confirm continued protocol eligibility before application of study drug.

8. Photographs taken before application of the Study drug (selected sites only).

9. Administration of study drug to all lesions including those lesions that may be newly developed. If any new lesions are not treatable, this will be documented by the team member who is applying the treatment.

10. Subjects will be given take-home instructions describing the potential local skin reactions and what to expect over the next 24 hours to several months.

11. Post treatment safety evaluations will be conducted by the research team via phone calls at 24 hours and days 7 and 14 after every treatment application (ERT). The phone call will review questions related to removal of Study drug, and review and documentation of local skin reactions, adverse events and con-meds since the prior visit or call. Phone calls may not be conducted by a research team member utilized as the subject's blinded assessor.

12. Depending on the age of the subject, the subject/guardian will wash off the Study drug 24 hours after application of Study drug. Subjects/guardian may gently remove the Study drug from lesions without the use of a washcloth in problematic areas prior to the directed 24 hours if the lesions have already blistered or if the subject is experiencing significant pain. Study drug should not be removed from the additional lesions, where possible, until the expected blistering occurs or the 24-hour time point is reached, whichever comes first.

- Exacerbation of a chronic or intermittent pre-existing condition, including an increase in frequency or intensity of the condition

- New conditions detected or diagnosed after investigational product administration, even if they were present before the start of the study

- Signs, symptoms, or the clinical sequelae of a suspected interaction with another medical product

- Local skin reactions (erythema, scaling/flaking/dryness, edema/swelling, small blisters, hyper- and hypopigmentation, scabbing/crusting, erosion/ulcerations, scarring)?

- Development of individual blisters that are greater than 20mm in diameter (the diameter of a dime). (An aggregated blister composed of a number of smaller blisters is not considered a severe blister)

- Blistering distal to the treatment site

- Scarring-(independent of any pigmentary changes; include depressed (atrophic) and elevated (hypertrophic)

- Secondary infection

The following are not examples of AEs:

- Medical procedures (The medical condition that led to the procedure as the AE should be reported.)

- Situations that are unwanted by the subject but in which an untoward medical occurrence did not occur, for example social inconvenience after admission to a hospital

- Anticipated day-to-day fluctuations of a preexisting disease or condition (present or detected before enrollment) that does not worsen overall

life-threatening, or require hospitalization but still may jeopardize the subject or may require medical intervention to prevent one of the outcomes listed in this definition. These events should also be considered serious. Examples of such events are intensive treatment in an emergency room or at home for allergic bronchospasm, blood dyscrasias, or convulsions that do not result in hospitalization.

An SAE requires additional detailed reports and follow-up. The content of these detailed reports must address the investigator's estimate of causality. The medical monitor will review the SAE to determine if it is an expected SAE (i.e., whether or not the SAE is identified in nature, severity, and frequency in the VP-102 Investigator's Brochure).

5.3 RECORDING ADVERSE EVENTS AND SERIOUS ADVERSE EVENTS

When an AE or SAE occurs, the investigator is responsible for reviewing all documentation (e.g., hospital progress notes, laboratory, and diagnostic reports, etc.) relative to the event(s). The investigator will record all relevant information about any AE (including SAEs) on the AE page of the eCRF. It is not acceptable for the investigator to send photocopies of the subject's medical records in lieu of the properly completed AE or SAE pages of the eCRF. These documents should not be sent unless they are specifically requested by the designated Medical Monitor. If this request occurs, all subject identifiers and protected health information should be blinded on the copies of the medical records before submission to the Sponsor and to the appropriate authorities.

The investigator will also attempt to report a diagnosis, instead of signs, symptoms, or other clinical information, for the AE. The diagnosis, not the individual signs and symptoms, should be documented on the appropriate page of the eCRF as the AE or SAE. In addition, SAEs need to be reported in the SAE report. AEs being processed as SAEs will also require additional documentation.

5.4 ASSESSMENT OF INTENSITY

The investigator will assess the intensity for each AE and SAE reported during the study. The assessment will be based on the investigator's clinical judgment.

The classifications in Table 2 should be used in assigning intensity of each AE recorded in the eCRF.

Table 2 Classification of AEs by Intensity

Intensity	Definition
Mild AE	An event that is easily tolerated by the subject, causing minimal discomfort and not interfering with everyday activities
Moderate AE	An event that is sufficiently discomforting to the extent of interfering with normal everyday activities
Severe AE	An event that prevents the subject from performing normal everyday activities

AE: adverse event.

Any AE that changes in intensity during its course will be recorded in the eCRF at the highest level experienced by the subject.

An AE that is assessed as severe should not be confused with an SAE. Severity is a category used for rating the intensity of an AE (such as mild, moderate, or severe myocardial infarction). However, the event itself may be of relatively minor medical significance, such as a severe headache. Both AEs and SAEs can be assessed as severe. An AE is considered serious (an SAE) when it meets one of the predefined outcomes described in Section 5.2.

Local Skin Reactions should be rated based on the severity ratings in the Local Skin Reaction Guide that is provided.

5.5 ASSESSMENT OF CAUSALITY

The investigator must estimate the relationship between the investigational product and the occurrence of each AE or SAE by using his or her best clinical judgment. Elements to consider for this estimate include the history of the underlying disease, concomitant therapy, other risk factors, and the temporal relationship of the event to the

5.7 REPORTING OF SERIOUS ADVERSE EVENTS

Any SAE occurring after the subject signs the informed consent form must be reported to the Sponsor or designee by phone, or e-mail within 24 hours of the time the investigator becomes aware of the SAE (Table). Urgent reporting of SAEs is required for the following reasons:

1. To enable the Sponsor to fulfill the reporting requirements to the appropriate regulatory authority

2. To facilitate discussion between the Sponsor and the investigator about appropriate follow-up measures (if necessary)

3. To facilitate the Sponsor's rapid dissemination of information about AEs to other investigators or sites in a multicenter study

4. To facilitate reporting unanticipated problems involving risk to subjects to the IRB

Table 4 Timeline for Reporting SAEs

Initial SAE Report		Follow-up SAE Report	
Time Frame	**Documents**	**Time Frame**	**Documents**
24 hours	SAE report	7 days	Updated SAE report

SAE: serious adverse event.

The SAE report must be completed as thoroughly as possible, including the following:

- Subject identification information
- Event term
- All available details about the SAE
- Causality of each SAE
- Signature of the investigator

Within 24 hours of knowledge of a new SAE, the investigative site will enter the event as an SAE into the EDC system being used for this study and recorded into the safety module. The SAE report should include the essential elements.

The SAE report will be forwarded to the Sponsor within the designated time frames. If additional information to complete the SAE report form is needed, the investigator will not wait before notifying the Paidion Medical Monitor via the SAE Hotline of the SAE. The SAE report form will be updated by the investigator when additional information is received.

New SAEs, or follow-up SAE information, may be reported to the Paidion Research Medical Monitor (Laurie Dunn, MD) by calling the SAE Hotline at (919) 928-6780. The SAE Hotline may be accessed 24 hours/day, 7 days/week. The Hotline is monitored 24 hours/day, 7 days/week. A call to the SAE Hotline is not required and does not alleviate the Investigator of the responsibility to report a new SAE in the EDC system within 24 hours of knowledge.

5.8 FOLLOW-UP OF ADVERSE EVENTS AND SERIOUS ADVERSE EVENTS

After the initial AE or SAE report, the investigator is required to follow each subject until the occurrence of one of the following:

- The condition resolves and/or stabilizes.
- The subject is lost to follow-up.
- 30-days after the end of study (EOS visit).

The appropriate SAE report form will be updated in the EDC once the SAE resolves, stabilizes, or is otherwise explained or until the subject is lost to follow-up. The investigator will also ensure that updates include any supplemental data that may explain causality of the SAE(s).

5.9 PREGNANCY

Should study personnel become aware of a subject's (or subject's partner's) pregnancy, the site personnel must report the pregnancy to the Sponsor's medical monitor within 24 hours by using the pregnancy notification form. The female subject will discontinue Study drug. The pregnancy will be followed until the outcome is known and will be reported to the Sponsor.

6.0 STUDY OR SITE TERMINATION AND SUBJECT DISCONTINUATION

6.1 SUBJECT DISCONTINUATION

Subjects are encouraged to complete the study; however, they may voluntarily withdraw at any time. The investigator will provide a written explanation of the reason for discontinuation in a source document and this information will also be recorded on the appropriate eCRF page. If a subject withdraws before completion, every effort should be made to complete the Day 84 assessments scheduled during the End of Study visit. Should a subject be unable to complete the in-office EOS evaluation by Day 100, if available, they may be given the option of an in-home assessment by a qualified member of the research team.

A subject may be removed from the study for the reasons described in Section 6.1.1 through Section 6.1.5.

6.1.1 Adverse Event

If a subject experiences an AE that, in the judgment of the investigator, the sponsor, or the medical monitor, presents an unacceptable consequence or risk to the subject, the subject may be discontinued from the study.

6.1.2 Intercurrent Illness

A subject may be discontinued from the study if, in the judgment of the investigator, the subject develops an intercurrent illness or complication that is not consistent with the protocol requirements or that, in any way, justifies withdrawal from the study.

6.1.3 Noncompliance

After the investigator, the medical monitor and/or study monitor consult (and the sponsor if appropriate), a subject may be discontinued from the study for the following administrative reasons:

- Failure to receive study medication or treatment as mandated by the specific instructions provided in Section 3.0

- Failure to comply with protocol requirements

6.1.4 Refusal of Investigational Product Administration

Any subject refusing clinical trial material for any reason will be discontinued from the study, and the reason(s) for their discontinuation will be documented on the appropriate eCRF page. Reasonable efforts should be made to monitor the subject for AEs and to complete follow-up assessments after treatment discontinuation. These efforts should be documented on the appropriate eCRF page.

6.1.5 Withdrawal of Consent

Any subject who withdraws consent for any reason at any time during the study will be discontinued from the study, and the reason(s) will be documented on the appropriate eCRF page. If subjects do not want their data that has already been submitted or specimens utilized they will need to submit a request in writing to the Investigator for removal of their information.

6.2 PREMATURE STUDY OR SITE TERMINATION

If the Sponsor, investigator, medical monitor, study monitor, or appropriate regulatory officials discover conditions arising during the study that indicate that the study should be halted or that the site should be terminated, this action may be taken after appropriate consultation among the Sponsor, investigator, medical monitor, and study monitor. Conditions that may warrant termination of the study include, but are not limited to, the following:

- The discovery of an unexpected, serious, or unacceptable risk to the subjects enrolled in the study

- A decision on the part of the Sponsor to suspend or discontinue testing, evaluation, or development of the product

A study conducted at a single site in a multicenter study may also warrant termination under the following conditions:

- Failure of the investigator to enroll subjects into the study at an acceptable rate

Name of sponsor company: Verrica Pharmaceuticals, Inc.

Name of finished product: VP-102 (0.7% w/v cantharidin)

Name(s) of active ingredient(s): Cantharidin

medical history) can occur up to 14 days before, or on the same day as Study drug application. Subjects that do not continue to meet criteria at Treatment Visit 1 will be discontinued and treated per standard of care. All lesions must be treatable at the time of randomization or the subject is not eligible to participate. Those subjects that meet the enrollment criteria will be randomized and treated with application of VP-102 or placebo to all molluscum lesions at Treatment Visit 1. Treatment will continue every 21 days to all treatable molluscum lesions until complete clearance or a maximum of 4 treatment sessions. The EOS study visit will be completed 21 days after Treatment Visit 4, (EOS; Day 84). In the event of scheduling conflicts in subsequent treatment visits, subjects may be scheduled 21 ± 4 days following their previous treatment for their next Treatment Visit and for their EOS visit.

In the event subjects miss a treatment visit and are outside the 4-day study window, they may return and be treated at the next available opportunity with the subsequent visit scheduled 21 days after the actual treatment visit. No study visits will be conducted after Day 100.

Inclusion criteria:
To qualify for inclusion in this study, subjects must:

1. Be healthy subjects, at least 2 years of age or older.
2. Consent to having all molluscum lesions treated and the physician must be willing to treat all molluscum lesions initially present. *Lesions within 10mm of the eyelid margins or the margin of any mucosal membrane should be evaluated carefully to ensure that they can be safely treated. Non-mucosal genital area lesions and inflamed lesions are considered treatable.*
3. Be otherwise medically healthy with no clinically significant medical history as determined by the investigator. *Subjects exhibiting active Atopic Dermatitis may be enrolled.*
4. On day of treatment refrain from application of all topical agents including alcohol-based sanitary products and sunscreens for a minimum of 4 hours before Study drug application. Topical agents including alcohol-based sanitary products and sunscreens may be used after application of the study drug so long as they are not applied within 5cm of treated skin lesions.
5. Refrain from swimming, bathing or prolonged immersion in water or any liquids until the Study drug is removed.
6. Have the ability or have a guardian with the ability to follow study instructions and be likely to complete all study requirements.
7. Provide written informed consent or assent in a manner approved by the institutional review board (IRB) and/or have a parent/guardian provide written informed consent as evidenced by the signature on an IRB approved assent/consent form.
8. Provide written authorization for use and disclosure of protected health information.
9. Agree to allow photographs to be taken, (selected sites only) of selected lesions at every visit that will be used for training, publication and future marketing brochures. *Photographs will be de-identified to those outside the research team. Efforts will be made to ensure that no photos with identifiable features are obtained.*

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phalerata). *Lytta vesicatoria*, a metallic green beetle, was primarily used as a source of cantharidin in the early 1900s, as it is endemic to the United States. Regardless of species of blister beetle, the structure of the cantharidin molecule is maintained with only variations in the quantity of compound that can be readily isolated. The *Mylabris* species of beetle contains a much greater concentration of cantharidin and is the primary type of beetle used in modern cantharidin preparations.

Cantharidin functions as a vesicant, weakening desmosomes in the epidermis when applied topically via a liquid film-forming formulation. Application to the skin causes the release of neutral serine proteases resulting in the destruction of intercellular desmosomes responsible for holding the layers of the skin together.[5] Intracellular tonofilaments are also weakened, the result being a fluid-filled, thin-walled epidermal vesicle. The superficial nature of the blisters is attributed to cantharidin's lesser effect on hemidesmosomes in the basal layer compared to the more superficial desmosomes. In almost all subjects, this process does not cause a scar, as the underlying dermal layer of skin is undamaged. Cantharidin has no known direct antiviral effects.

Many physicians prefer cantharidin to other therapies for the treatment of molluscum such as cryotherapy, curettage or pricking individual lesions with subsequent expression of molluscum bodies because it is painless upon application, requires only limited treatment cycles for significant lesion reduction or complete resolution and is well-tolerated by subjects, most of whom are children. Furthermore, cantharidin's long history of use has provided strong evidence of its safety when applied topically.

Although cantharidin has been used extensively for decades in the treatment of several dermatologic conditions including molluscum and verruca vulgaris, specifications for the quality of active pharmaceutical ingredient or a standardized formulation have never been established. Furthermore, a lack of reliable and regulated vendors of the compounded drug increases the chance of the drug product being inappropriately prepared, tested, stored or applied, which in turn increases the potential for unintended or even dangerous consequences in the future. Most currently used cantharidin preparations are prepared as 0.7% w/v (weight/volume) solutions in an acetone solvent with a flexible-collodion base in a screw-top glass bottle at volumes intended for repeated use across multiple subjects by the medical professional. This type of container closure system paired with highly volatile formulations presents multiple challenges. Current clinical practice, which reuses the same bottle on multiple patients,

as part of the Evaluation of Response to Treatment (ERT) with type and intensity recorded on the AE log: blistering, pain, pruritus, erythema, edema, erosion/ulcerations, flaking/scaling/dryness, scabbing/crusting, and pigmentation changes (hyperpigmentation or hypopigmentation). Scarring will be assessed at each treatment visit and the EOS visit by a qualified medical professional. Scarring information will not be collected as part of the phone assessment. Additional information related to AE's and ConMeds will also be collected during each assessment.

Subject quality of life and measure of impact of skin disease will be collected using the Children's Dermatology Life Quality Index Questionnaire. The CDLQI questionnaire is validated for use in children ages 4-16 years of age but will be administered to all study subjects and/or their guardians regardless of age. It should be handed to the subject who is asked to fill it in with the help of a parent/guardian as needed. The subject or guardian will be given completion instructions to evaluate their skin condition as it specifically relates to molluscum contagiosum. They will be guided to disregard the impact of any other concomitant skin conditions like atopic dermatitis during completion. The CDLQI should be scored by the site using the guidelines in Appendix 1.

Subjects will be given take-home instructions describing the potential local skin reactions and what they might expect throughout the course of the study. The instructions include recommendations for wound care, when it is important to call their doctor, who to contact in the event of emergency and a 24-hour emergency number. The additional scheduled visits and calls up through the next treatment visit, or EOS, will also be indicated on this form. Take-home instructions will be reviewed and provided at each treatment visit.

To assist the research team in the ERT phone calls, education materials in the form of a local skin reaction guide with specific photos identifying the various skin reactions and examples of intensity will be reviewed at the clinic with the subject/guardian by the research team. Should a subject report experiencing excessive blistering or another adverse event needing physician assessment during the ERT call, they will be scheduled for an unplanned study visit and safety evaluation as soon as possible.

Subjects 18 and older must provide consent as required by the IRB before any study procedures are conducted. Parents or guardians must provide informed consent, and pediatric subjects older than 10 years must provide assent as required by the IRB before

- If the subject discontinues the study prematurely (after the first treatment) for any reason, attempts will be made to encourage the subject/guardian to complete the EOS assessments. At home assessments by a trained member of the study team may be considered in order to complete the EOS assessment.

- Subjects will be monitored for signs and symptoms of AEs throughout the study. All AEs (including LSRs) will be reported in the electronic case report form (eCRF), including seriousness, severity, action taken, and relationship to the Study drug. If AEs should occur, the first concern will be the safety of the subject.

- Assessment of LSRs will be recorded at each Treatment Visit using the protocol specific ERT form. Additional assessments will be conducted at 24-hours as well as day 7 and 14 after treatment either in person or by phone contact using the ERT form. LSRs will be considered AEs even though some LSRs may be part of the normal response to treatment and correlated with efficacy. The following LSRs will be recorded: blistering, pain, pruritus, erythema, edema, erosion/ulcerations, flaking/scaling/dryness, scabbing/crusting, and pigmentation changes (hyperpigmentation or hypopigmentation). These responses will be queried for duration and intensity. Scarring will be evaluated in person by a qualified practitioner who is a trained member of the research team at in office treatment visits and the EOS visit.

- Medical interventions taken throughout the course of the study prior to initial treatment, at 24-48 hours and 7, 14 and 21 days after treatment.

2.3.2 Efficacy

Efficacy parameters will be recorded for all randomized subjects. Clinical response to treatment of molluscum lesions will be evaluated at each scheduled visit until EOS by counting all treatable molluscum lesions. Untreatable lesions will be tracked and recorded.

2.4 RANDOMIZATION AND BLINDING

Randomization through an interactive web response system (IWRS) will be used to assign treatment in a 3:2 ratio (expected 150 subjects treated with VP-102 to 100 subjects treated with placebo). Trial sites will have access to an internet-based randomization system. Randomization will be conducted in a centralized manner.

vehicle in a hot or cold environment). Contact the study sponsor in the event you believe that any materials may have been exposed to such conditions for guidance. Study drug may be administered only by the investigator or by a trained member of the clinical site staff specifically as authorized by the investigator.

3.4 CONCOMITANT MEDICATIONS

All medications taken within 14 days prior to the first dose of the Study drug will be classified as prior medication; while all medications used after the first dose of Study drug will be classified as concomitant medications. Prior and concomitant medications will be recorded in the eCRF, along with the reasons for administration and durations of use.

Medications or treatments that can interfere with the evaluation of the Study drug [e.g., topical steroids, PDE-4 inhibitors (such as Eucrisa®), and calcineurin inhibitors (pimecrolimus, tacrolimus)] should not be used on the day of treatment and should not be applied within 5cm of treated skin lesions. Particular attention will be paid to treatments that can influence the intended effects or mask the side effects of the Study drug (e.g., topical steroids). Lotions and creams such as sunscreens should not be used for a minimum of 4 hours before treatment and should not be applied within 5cm or on treated skin for 24 hours following treatment. Immunizations and flu shots may be administered throughout the study but not within 5 days before or after treatment.

4.2 MEASUREMENTS AND EVALUATIONS

4.2.1 Screening Period (Up to 14 days prior to Treatment Visit 1)

Before the initiation of screening assessments, the subject/guardian must be given a complete explanation of the purpose and evaluations of the study. Subsequently and depending on the age of the subject, the subject/guardian must sign and receive a copy of an informed consent form (ICF) (Section 7.3), an IRB-required assent form (subjects 10 years or older), and an authorization for use and disclosure of protected health information (Section 7.3) that was approved by the IRB. Once consent and assent is obtained, the Screening Period assessments will be performed. Subjects will be screened within 14 days prior to or on Treatment Visit 1 of the study. Following consent and assent, review and recording of any medical history will take place, and the following evaluations will be performed and recorded in the electronic case report form (eCRF):

1. Demographics (date of birth, sex, ethnic origin).
2. Height and weight
3. Prior relevant medical history
    a. All past relevant illnesses with in the past 5 years.
    b. All drugs used (including non-prescription and herbal [complementary medicine] products) within 14 days prior to screening procedures. Any anti-microbial, anti-viral, steroidal or topical drugs received within 30 days prior to Day 1.
    c. Any non-pharmacologic treatments (e.g., ice packs, heat packs, warm soaks, etc.) administered in the 72 hours prior to the application of the Study drug.
4. Molluscum contagiosum history (duration and previous treatments). If treated with cantharidin, confirm date of last treatment.
5. Limited physical examination.

4.2.4 End of Study (Day 84):

Subjects will return to the clinical site for:

1. Review and recording of any concomitant medications and non-pharmacologic treatments/procedures since previous visit.
2. Review and recording of any AEs.
3. Vital signs (heart rate and temperature) obtained at the beginning of visit.
4. Limited physical examination.
5. Lesions counted and recorded by blinded assessor.
6. CDLQI assessment
7. Dermatologic exam, ERT assessment (LSRs, AEs, ConMeds) (conducted by qualified member of the research team who is not utilized as a subject's blinded assessor.
8. Urine pregnancy test for females of childbearing potential.
9. Photographs (at selected sites only).

5.0 PROCEDURES FOR HANDLING ADVERSE EVENTS AND SERIOUS ADVERSE EVENTS

5.1 DEFINITION OF AN ADVERSE EVENT

The following definition of *adverse event* (AE) will be used for this study:

> Adverse event means any untoward medical occurrence associated with the use of a drug in humans, whether or not considered drug related.

An AE can be any unfavorable and unintended sign, symptom, or disease (new or exacerbated) temporally associated with the use of the investigational product, regardless of whether it is considered to be related to the investigational product.

The following are examples of AEs:

- Expected progression of the disease being studied, including signs or symptoms of the disease, unless progression is more severe than expected for the subject's condition

AEs may include pre-treatment or post-treatment events that occur as a result of protocol-mandated procedures (e.g., invasive procedures, modification of the subject's previous therapeutic regimen). AEs should be captured even if they occur during periods without drug treatment or post-treatment periods. AE collection begins once the subject has signed informed consent and will continue until the EOS visit has been completed.

The investigator is responsible for performing periodic and special assessments for AEs. The investigator and study personnel will note all AEs mentioned by the subject starting from the day the informed consent is signed until the end of study visit (~Day 84). All clinical complaints volunteered by or elicited from the subject or parent/guardian during the study will be recorded on the appropriate page of the eCRF for the study period indicated. The subject will receive appropriate treatment and medical supervision for any AE that occurs.

All unresolved AEs will be followed for 30 days after study completion. All AEs will be summarized in the annual report or more frequently if requested by the regulatory agency. SAEs require special reporting in addition to documentation in the eCRF as described in Section 5.3.

investigational product. The investigator will also consult the Investigator's Brochure or product label for marketed products in estimating the relationship.

Because of reporting timelines, the investigator might have minimal information to include in the initial SAE report. However, the investigator must always make an assessment of causality for every SAE before the transmission of the SAE report. The investigator may change his or her opinion of the causality in light of follow-up information, with subsequent amendment of the SAE report. Causality assessment is one of the criteria used to determine regulatory reporting requirements and should not be left blank in the SAE report. The same applies to AEs that are to be processed as SAEs. Some definitions to use in the assessment are provided in Table 3.

Table 3 Assessment of Causality of AEs

Term	Definition
Definitely related	The AE *is clearly related* to the investigational agent(s) or research intervention: the AE has a temporal relationship to the administration of the investigational agent(s) or research intervention and follows a known pattern of response, and no alternative cause is present.
Possibly related	The AE *may be related* to the investigational agent(s) or intervention: the AE has a temporal relationship to the administration of the investigational agent(s) or research intervention and follows a suspected pattern of response, but an alternative cause is present.
Probably related	The AE is *likely related* to the investigational agent(s) or intervention: the AE has a temporal relationship to the administration of the investigational agent(s) or research intervention and follows a known or suspected pattern of response, but an alternative cause may be present.
Unrelated (or not related)	The AE is *clearly not* related to the investigational agent(s) or intervention: the AE has no temporal relationship to the administration of the investigational agent(s) or research intervention, and follows no known or suspected pattern of response, and an alternative cause is present.

AE: adverse event.

5.6 EXPECTEDNESS OF SERIOUS ADVERSE EVENTS

An expected AE is one that is consistent with the known risk information described in the product label (if applicable) or the current Investigator's Brochure. The expectedness of an SAE will be assessed by the medical monitor or sponsor on receipt of the initial SAE report.

- Failure of the investigator to comply with pertinent regulations of appropriate regulatory authorities

- Submission of knowingly false information from the site to the sponsor, study monitor, or appropriate regulatory authority

- Insufficient adherence to protocol requirements

Study termination and follow-up will comply with the conditions set forth in International Council for Harmonisation E6, Guideline for Good Clinical Practice. Data from all sites, including those that have been terminated for non-compliance or unsatisfactory enrollment will be evaluated and included in the interpretation of study findings. Subjects from sites that terminate early will be considered for analysis. If a subject does not complete the study, they will still be counted as a failure for the primary endpoint.