

1.0 PROTOCOL SUMMARY

Protocol Number/ Title:	IM01-102: A Multi-Center, Open-Label, Extension Trial for the Intratumoral Injection of VCL-IM01 Followed by Electroporation in Metastatic Melanoma
Trial Design:	Open-Label, Multi-Center Trial.
Objective:	To evaluate the safety of multiple courses of intratumoral injection of VCL-IM01 followed by electroporation.
Investigational Product:	IL-2-encoding plasmid formulated in phosphate-buffered saline at 0.5 mg/mL, 1.5 mg/mL, or 5.0 mg/mL (VCL-IM01) intratumorally injected and followed by electroporation with Inovio MedPulser [®] 1.0 cm array with needles up to 3 cm long (one 6-pulse cycle per tumor).
Primary Endpoint:	Safety of multiple courses of intratumoral injection of VCL-IM01 followed by electroporation in subjects with recurrent metastatic melanoma.
Secondary Endpoints:	Overall response rate, duration of response, treated tumor response rate, assessment of injected tumor(s) for induration, inflammation, and erythema.
Trial Population:	Subjects with recurrent metastatic melanoma that have achieved stable disease, partial or complete response through Week 18 while under treatment in the Vical sponsored IM01-101 trial.
Key Inclusion Criteria:	<ul style="list-style-type: none"> • Completed treatment under IM01-101 protocol with an outcome of stable disease, partial or complete response. • Histologically proven recurrent metastatic melanoma in a previous complete responder • Tumor(s) to be treated must be at least 1 cm², less than 25 cm², and be accessible to treatment. • ECOG performance status of 0 or 1 • Not currently receiving chemotherapy or immunotherapy • Platelet count $\geq 100,000/\text{mm}^3$. • Serum creatinine ≤ 2.0 mg/dL. • White blood cell count $\geq 2500/\text{mm}^3$. • Negative pregnancy test for women of child-bearing potential. • Men and women (of child-bearing potential) must agree to use an appropriate method of birth control. • Able and willing to give informed consent.

<p>Key Exclusion Criteria (continued):</p>	<ul style="list-style-type: none"> • Subjects who are candidates for curative surgery. • Diabetes • Evidence of significant active infection at the time of study entry. • Subjects receiving concurrent anticancer therapy, any immunosuppressive treatment or any other investigational therapy. • Pregnant or lactating. • Subjects with significant cardiac arrhythmias, electronic pacemakers, defibrillators, or any other implanted electronic device. • Subjects with other diseases (e.g., an underlying autoimmune disorder) which, in the Investigator’s opinion, could result in serious or life-threatening complications.
<p>Contraindications for Electroporation:</p>	<ul style="list-style-type: none"> • Do not use when metal implants are within the treatment area. • Do not use on tumors that invade bone. • Do not use on tumors that invade or envelop major blood vessels or nerves.
<p>Dose Regimen and Assessments:</p>	<p>Each subject will undergo a course of therapy that consists of two 7-week cycles (includes 4-week treatment period consisting of weekly treatments, followed by a 3-week safety observation period). Each subject will receive the highest dose known to be safe and available at the time of treatment. Potential doses are:</p> <p style="padding-left: 40px;">0.5 mg, 1 tumor, once weekly x 4 1.5 mg, 1 tumor, once weekly x 4 5.0 mg, 1 tumor, once weekly x 4 5.0 mg, 3 tumors (15 mg), once weekly x 4</p> <p>Each dose is administered by intratumoral injection and followed by electroporation.</p> <p>Subjects will be eligible to receive up to two courses of treatment if the investigator has determined that the subject has stable disease or has achieved either a partial or complete response..</p>
<p>Pre-medication</p>	<p>No intratumoral local anesthetic or general anesthesia is allowed. Subjects may receive topical anesthetics or conscious sedation (for example, Versed®) if needed.</p>
<p>Evaluations</p>	<p>Safety will be assessed throughout the trial at every visit.</p> <p>Tumor measurements and standardized serial photography will be completed at Weeks 7 and 14 of each treatment course. Determination of response by RECIST criteria will be conducted at Week 14 of each treatment course.</p> <p>Safety labs will be collected throughout the trial; at screening and Week 3 of the first cycle, and on the first and last injection date of each subsequent cycle.</p>