Synopsis

Name of Sponsor/Company: Vascular Biogenics, Ltd	**Name of Finished Product:** VB-201	**Name of Active Ingredient:** VB-201

Title of Study: A Randomized, Double-Blind, 12-Week, Dose-Ranging, Placebo-Controlled Study to Evaluate the (1) the Efficacy and Safety of Oral VB-201 in Patients with Moderate to Severe Plaque Psoriasis and (2) the Effect of Oral VB-201 on Carotid Artery and Ascending Aorta Positron Emission Tomography (PET) [18]F-fluorodeoxyglucose (^{18}FDG) Uptake in Psoriasis Patients with Abnormal Baseline PET ^{18}FDG Scans

Investigators in:
Germany, Israel and United States

Study Center(s):
See Appendix 16.1.4 (not applicable)

Publications (reference): None

Study Period: Date first patient dosed: 08 JAN 2010 Date last patient completed: 22 JUL 2011	**Phase:** 2

Objectives:

Safety Objective:

- To examine the safety and tolerability of 12 weeks' treatment with VB-201 or placebo in patients with psoriasis.

Efficacy Objective:

- To examine the effect of 12 weeks' treatment with two different doses of VB-201 compared to placebo on measures of disease activity in patients with psoriasis.

PET Sub-Study Objective:

- To examine the effect of treatment with 20 mg/day and 80 mg/day VB-201 on carotid artery and ascending aorta plaque inflammation as measured by PET-CT ^{18}FDG uptake measured by a target to background ratio (TBR), in psoriasis patients with an elevated baseline TBR.
-

Methodology:

This was a double-blind, parallel-group, randomized, proof-of-concept study with 12 weeks of daily oral administration of VB-201 at doses of 20 mg/day or 80 mg/day or placebo.

Patients were screened for eligibility and, up to 28 days later at the baseline visit, randomized to one of three treatment groups (1:1:1): VB-201 20 mg/day: VB-201 80 mg/day: placebo/day.

Each patient had a final evaluation 4 weeks after stopping treatment with study drug.

For the sub-study, patients who met the eligibility criteria for the main study at the sub-study sites and also met inclusion criteria for the sub-study and signed an informed consent, had a PET-CT of the neck and thorax at the Baseline visit. Patients with a PET-CT ^{18}FDG uptake with a target to background ratio (TBR) ≥1.6 in either the carotid artery or the ascending aorta qualified for one additional PET-CT scan at Week 12. Patients with a TBR <1.6 in both the carotid artery and ascending aorta were not eligible for the additional PET-CT scan at Week 12, but could remain in the study, if otherwise eligible.

Low-potency corticosteroids (Class 6 or 7 in the National Psoriasis Foundation potency chart) were permitted on the scalp, palms, soles, axilla, and groin during this study, except on days of study visits. Emollients (on any lesions) and tar-based shampoos were also permitted except on days of study visits.

Name of Sponsor/Company: Vascular Biogenics, Ltd	**Name of Finished Product:** VB-201	**Name of Active Ingredient:** VB-201

Other treatments for psoriasis (including other topical and systemic psoriasis treatments, phototherapy and biologic treatments) were prohibited, as mentioned in the eligibility criteria.

An Independent Data monitoring Committee (IDMC) was responsible for the review of the safety data for this study, according to a pre-specified charter.

Number of Patients (Planned and Analyzed):

Planned:

The main study was conducted worldwide. It was anticipated that approximately 180 patients would be enrolled into the main study (including patients also participating in the sub-study). Anticipating a drop-out rate of approximately 17%, it was expected that a total of 150 evaluable patients, 50 in each treatment group. In the sub-study, it was anticipated that a total of 75 patients would be randomly assigned at a 1:1:1 ratio to one of three treatment groups (placebo, 20 mg/day VB-201, or 80 mg/day VB-201) with 25 patients randomized to each group. Anticipating a drop-out rate of approximately 22%, it was expected that a total of 60 patients, 20 in each treatment group, would complete this sub-study.

Analyzed:

A total of 185 patients were randomized into the main study (75 of them into the sub-study): 66 to the VB-201 20 mg group, 59 to the VB-201 80 mg group, and 60 to the placebo group. All randomized patients (except for one placebo patient who wasn't treated) were included in the Safety Population defined as patients who received at least one dose of study medication. Five patients (4 assigned to VB-201 20 mg and one placebo patient) were excluded from the modified intent-to-treat (MITT Population) analyses; these patients either had no Psoriasis Area and Severity Index (PASI) data available at baseline or no PASI data were available at any post-baseline visit.

In addition to those patients excluded from the Safety Population and MITT populations, six additional patients (2 in each of the 3 treatment groups) were excluded from the Per-Protocol Population analyses.

Of the 75 patients who enrolled into the sub study, 71 underwent a baseline PET-CT scan, 58 were eligible for the week-12 PET-CT and 47 completed the sub-study and were evaluable for analysis.

Diagnosis and Main Criteria for Inclusion:

Inclusion Criteria:

1. Fully understand all elements of and have signed and dated the written Institutional Review Board (IRB) or Independent Ethics Committee (IEC) approved informed consent before initiation of protocol-specified procedures;
2. Male or female patients, ≥18 to ≤75 years of age, who had a diagnosis of chronic plaque psoriasis for at least 6 months;
3. Non-anorexic patients with a body mass index (BMI) ≥20;
4. PASI score of ≥12;
5. Plaque psoriasis covering ≥10% of body surface area (BSA);
6. Psoriasis severity at least moderate, scoring at least 3 on a 0 to 4 point Physician Global Assessment (PGA) scale;
7. For a female patient; either:
    - patient was of non-childbearing potential, defined as: menopause with amenorrhea >2 years, hysterectomy, or bilateral oopherectomy; or
    - agreed to continue to use adequate contraception (implants, injectables, combined oral contraceptives, intrauterine devices [IUDs], sexual abstinence or vasectomised partner) throughout the study and for at least one month following termination and had a negative pregnancy test at screening and before the first dose of study drug;

    Males must have used at least one method of contraception (e.g., condom) throughout the study;

Name of Sponsor/Company: Vascular Biogenics, Ltd	**Name of Finished Product:** VB-201	**Name of Active Ingredient:** VB-201

8. In the opinion of the Investigator, the patient was compliant and had a high probability of completing the study and all required procedures.

In addition to the inclusion criteria listed for the main study, the following inclusion criteria were met to enroll in the sub-study:

1. Presence or history of at least one of the following:
   - Non-insulin dependent diabetes mellitus (NIDDM), peripheral vascular disease (PVD), smoker, presence or history of hypertension, obesity (BMI ≥25), hypercholesterolemia (LDL>160 or taking anti-hyperlipidemia treatment), or family history of ischemic heart disease (in brother or father before age 55, in sister or mother before age 65) or,
   - At least 40 years of age with a history of psoriasis for at least 7 years or,
   - Presence of ischemic heart disease or cerebrovascular disease;
2. Able to medically tolerate the procedures and medications involved in the performance of the imaging studies;
3. Carotid and/or ascending aorta plaque inflammation as suggested by an uptake TBR ≥1.6 as determined by baseline ^{18}FDG PET-CT scan.

Exclusion Criteria:

1. The patient presented with the predominant type of psoriasis as guttate, erythrodermic, inverse, pustular or palmo-plantar or an unstable form of psoriasis;
2. Received any investigational drug within 30 days of screening;
3. The patient had not undergone wash-out periods of sufficient duration for the following treatments at Baseline:
   - Topical psoriasis treatments: 2 weeks;
   - Systemic psoriasis treatments: 4 weeks or 5 half-lives (whichever was longer);
   - Phototherapy: 4 weeks.
4. The patient anticipated getting enough ultra-violet light during the study (e.g. sunbathing; tanning salon, etc.) to cause psoriasis to improve;
5. The patient had a known allergy or sensitivity to the study treatment(s) or to any of the excipients contained in the study drug formulation;
6. Any other acute or chronic medical condition that, in the opinion of the Investigator, increased the risk to the patient or the likelihood that the patient would be unable to complete the study;
7. Patients with any laboratory test at screening that common medical practice would deem as significantly abnormal. The following were deemed as significantly abnormal:
   - alanine transaminase (ALT), aspartate transaminase (AST), or alkaline phosphatase ≥1.5-times the upper limit of normal (ULN) or
   - cytopenia (to include any of the following: WBC $<3.5\times10^3/\mu L$; Hgb <10 g/dL; platelets $<120\times10^3/\mu L$; neutrophils absolute $<1.5\times10^3/\mu L$; lymphocytes absolute $<0.8\times10^3/\mu L$) or
   - Creatinine ≥1.25-times the upper limit of normal (ULN);

   If, in the Investigator's opinion, there was no reason for the test result(s) to be abnormal, the abnormal test(s) may have been repeated once during the screening period.
8. History of cancer, the exception was skin cancer, see below.

Name of Sponsor/Company: Vascular Biogenics, Ltd	**Name of Finished Product:** VB-201	**Name of Active Ingredient:** VB-201

- Patients with >3 previous squamous cell skin cancer lesions were excluded;
- Patients who had histologically controlled excision of basal cell and/or squamous cell carcinoma of the skin and had been declared to have no evidence of tumor could be enrolled;
- Patients who had basal cell and/or squamous cell carcinoma of the skin removed and had not met these criteria could be enrolled if the skin cancer was removed >3 years prior to study participation and there was no evidence of recurrence.

9. Had a clinically significant systemic infection (e.g., chronic or acute infection, urinary tract infection [UTI], upper respiratory infection [URI]) within 30 days of Day 0, or a history or presence of recurrent or chronic infection (e.g. viral infections, [including hepatitis B or C, human immunodeficiency virus (HIV)], bacterial infections, systemic fungal infections, or syphilis);
10. Evidence of tuberculosis, as indicated by a positive tuberculin skin test (defined as ≥10 mm induration) or a quantiferon test in patients known to have a + purified protein derivative (PPD) and a negative chest x-ray at screening or prior to screening;
11. History of substance abuse, including alcohol abuse, within the past year;
12. Had a history of or had a current, clinically significant major psychiatric disorder (e.g., major depressive disorder, psychosis, schizophrenia) according to the criteria of the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV-TR) [Exception: patients with depression that had been adequately controlled for at least 6 months could enroll in the study];
13. History of clinically significant hypoglycemia;
14. Patients with currently active peptic ulcer or gastroesophageal reflux disease;
15. Female patient with a positive pregnancy test or nursing, or planning a pregnancy during the course of the study;
16. Unwillingness to use reliable and acceptable contraceptive methods (e.g. implants, injectables, combined oral contraceptives, IUDs, sexual abstinence or vasectomised partner) throughout the study and for at least one month following termination, except for female patients who were surgically sterile (post hysterectomy or at least 1 year post tubal ligation) or at least 2 years postmenopausal;
17. Patients with a QTc-prolongation > 470 msec, risk factors for torsades de pointes such as heart failure New York Heart Association (NYHA) II-IV, hypokalaemia, family history of long QT syndrome and patients using concomitant medication that prolongs the QT interval;
18. Unwilling or unable to comply with study requirements.

In addition to the exclusion criteria for the main study, patients meeting any of the following were excluded from participation in the sub-study:

1. Recent (within 3 months prior to the Baseline visit) clinically significant coronary event, including unstable angina pectoris, myocardial infarction, angioplasty, or coronary artery bypass grafting;
2. Patient too agitated, uncooperative, or claustrophobic to remain still for PET-CT acquisition
3. Patient with fasting blood glucose level >200 mg/dL.

Test Product, Dose and Mode of Administration

VBL has developed a phospholipid analog, VB-201 (formerly CI-201), a small molecule which belongs to a new class of compounds termed lecinoxoids. VB-201 is an immunomodulator working specifically on antigen presenting cells and endothelial cells via specific receptors and signaling pathways. Thus VB-201 reduces the levels of inflammatory cytokines and impairs chemotaxis of inflammatory cells.

Name of Sponsor/Company: Vascular Biogenics, Ltd	**Name of Finished Product:** VB-201	**Name of Active Ingredient:** VB-201
The final product is encapsulated in hard gelatin capsules. Patients took a single capsule of 20 mg or two 40 mg capsules (80mg dose) of VB-201 every morning with breakfast for 12 weeks.		
Duration of Treatment: Patients participated in the study for approximately 20 weeks: up to 4 weeks for screening and establishment of baseline followed by 12 weeks of blinded treatment (VB-201 at 20 mg/day or 80 mg/day, or placebo), and a follow-up visit 4 weeks after their last dose of study medication.		
Reference Therapy, Dose and Mode of Administration: Placebo was blinded to match VB-201 in appearance. Patients took placebo capsules every morning with breakfast for 12 weeks.		
Criteria for Evaluation: The Safety Population included patients who received at least one dose of study medication. This population was used in all safety reporting and analysis. For the purposes of this Phase II study, an MITT Population was utilized for all efficacy analyses and included all patients randomized who received at least one dose of study medication, had an efficacy evaluation (i.e., PASI score) at baseline, and had at least one efficacy evaluation after study treatment began. Patients in the MITT Population who did not have major protocol deviations or non-compliance formed the PP Population.		
Efficacy: **Primary Efficacy Endpoint:** Proportion of patients in each of the VB-201 dose groups who achieved at least 75% improvement in the PASI from baseline at Week 12 (PASI 75) compared to the proportion of PASI 75 responders in the placebo group. **Secondary Efficacy Endpoints:** 1. Proportion of patients in each of the two VB-201 treatment groups who achieved at least 50% improvement in the PASI from baseline at Week 12 (PASI 50) compared to the proportion of PASI 50 responders in the placebo group; 2. Proportion of patients in the two VB-201 treatment groups combined who were PASI 75 responders at Week 12 compared to the proportion of PASI 75 responders in the placebo group; 3. Change in affected BSA from baseline to Week 12 in each of the VB-201 treatment groups compared to placebo; 4. Change in PGA scores from baseline to Week 12 in each of the VB-201 treatment groups compared to the placebo group; 5. Change in Patient Psoriasis Global Assessment scores from baseline to Week 12 in each of the VB-201 treatment groups compared to the placebo group; 6. PASI and PGA responses for all groups from Week 0 to Week 12. **Sub-study Endpoints:** The maximum TBRs in individual plaques were analyzed and averaged for each treatment group at baseline and Week 12. The efficacy variables in the PET-CT sub-study are as follows: <u>Primary</u>		

Name of Sponsor/Company: Vascular Biogenics, Ltd	**Name of Finished Product:** VB-201	**Name of Active Ingredient:** VB-201

- Change of the mean of the maximum Target Background Ratio (TBR) in the MDS from baseline to Week 12 for the index vessel.

Secondary

- Change of mean of maximal TBR values measured from baseline to Week 12 for the index vessel, the left and right common carotid arteries and the ascending aorta;
- Change of mean of mean TBR values measured from baseline to Week 12 for the index vessel, the left and right common carotid arteries and the ascending aorta;
- Change of mean of the maximum TBR in the MDS from baseline to Week 12 for the left and right common carotid arteries and the ascending aorta

Each of these efficacy variables were analyzed in the PET-CT Sub-Study Population in two different ways:

(i) Within each of the three treatment groups and for each vessel, the null hypothesis that there is no change from Baseline to Week 12 (i.e. a change equal to zero) was tested by a two-sided test at the 5% significance level.

(ii) For the VB-201 80 mg/day and the VB-201 20 mg/day groups the null hypothesis that there is no difference in the change from baseline to Week 12 compared to placebo was tested by a two-sided test at the 5% significance level. This analysis was based on an ANCOVA model with baseline value as covariate.

Index vessel is defined as vessel with highest uptake at baseline for which there is follow-up data of acceptable quality.

Pharmacokinetics Parameters:

Blood samples for measurement of VB-201 trough plasma concentrations were obtained from patients at Baseline, Weeks 4, 8, and 12/ET.

Safety:

Safety was assessed by adverse events (AEs), vital signs, physical examinations, electrocardiograms (ECGs) and laboratory testing (blood hematology, blood chemistry, urine analysis).

Name of Sponsor/Company: Vascular Biogenics, Ltd	**Name of Finished Product:** VB-201	**Name of Active Ingredient:** VB-201

Statistical Methods (Main Study):

The primary efficacy analyses were completed in the MITT Population. Efficacy analyses were also completed for a Per-Protocol Population. . Categorical data are presented as counts and percentages. Continuous data are presented as summary statistics. All statistical comparisons are two-sided at the 5% level of significance. No adjustments to the level of significance were made for multiple comparisons.

The primary efficacy analysis was performed on the MITT Population and compared the proportions (%) of patients achieving a PASI 75 response as defined in Section 6.4.1 in the VB-201 80 mg/day group to the placebo group at Week 12 and in the VB-201 20 mg/day group to the placebo group at Week 12. Non-responder imputation was utilized for these MITT population analyses, i.e. patients who drop out before week 12 for any cause and patients with missing PASI score at Week 12 were considered to have no PASI 75 response at Week 12.

These analyses were performed using the Cochran-Mantel-Haenszel (CMH) chi-square test stratified by country. The null hypothesis of equality of PASI 75 response rates was assessed using two-sided tests at the 5% level of significance. No adjustment for multiplicity was performed due to the exploratory nature of this Phase II study.

The primary efficacy analysis of PASI 75 response was supported by two further analyses:

1) Comparison of the proportions of patients achieving a PASI 75 response in the pooled VB-201 groups to the placebo group at Week 12. As the primary analysis this analysis was performed by a two sided CMH test stratified by country at the 5% level of significance.
2) A dose-response analysis of VB-201 utilizing the proportion of patients achieving a PASI 75 response at Week 12 in the VB-201 80 mg/day and 20 mg/day treatment groups and the placebo group was carried out using a two-sided CMH row mean score test stratified by country at the 5% level of significance. For the test it was assumed that the treatment groups (placebo, VB-201 20 mg/day, and VB-201 80 mg/day) are equally spaced.

Secondary efficacy endpoints and analyses were:

- PASI 50 response at Week 12 in each of the two VB-201 treatment groups compared to placebo. This efficacy variable was analyzed the same way as the PASI 75 response at Week 12, including an analysis with pooled VB-201 groups and a dose-response analysis;
- Change in affected BSA from baseline to Week 12 in each of the two VB-201 treatment groups compared to placebo;
- Change in PGA scores from baseline to Week 12 in each of the two VB-201 treatment groups compared to placebo;
- Change in Patient's Psoriasis Global Assessment scores from baseline to Week 12 in each of the two VB-201 treatment groups compared to placebo.

For each of these efficacy variables, the hypotheses of no difference in change from baseline to Week 12 between the VB-201 80 mg/day group and placebo and between the VB-201 20 mg/day group and placebo was tested at the 5% level of significance by two-sided tests coming from an ANCOVA with baseline value and country as additional covariates. Missing values were imputed by the Last Observation Carried Forward approach (LOCF) i.e., the observation from the last preceding visit with a non-missing value (including baseline and disregarded visits) was used.

Additionally, based on feedback from the study steering committee, ad hoc analysis were performed on the secondary endpoints of PGA and Patient Global Assessment (PtGA) assessed as ordinal variables, using a two-sided CMH and also a proportional odds model,

Statistical Methods (Sub- Study):

Name of Sponsor/Company: Vascular Biogenics, Ltd	**Name of Finished Product:** VB-201	**Name of Active Ingredient:** VB-201

All statistical assumptions made for the main study were applied to all sub-study analyses.

All patients enrolled in this sub-study and who had a baseline PET-CT measuring plaque Target to Background Ratio (TBR) of the aorta and carotid arteries and a follow-up PET-CT scan measuring plaque TBR at 12 weeks were included in the statistical analysis evaluating the effect of VB-201 on TBR.

Descriptive statistics were provided for plaque TBR, change from baseline and percent change from baseline at Week 12 for patients who received VB-201 20 mg/day, VB-201 80 mg/day, and placebo.

The actual change from baseline and percent change from baseline in plaque TBR were analyzed between patients who received active versus placebo study drug. An ANCOVA using baseline value as a covariate was used to determine if there was a dose-related effect of VB-201 at 12 weeks.

Within dose group changes from baseline were analyzed for each visit. A paired T-test was used to evaluate the difference at 12 weeks.

Rationale for Number of Patients in Main Study:

The sample size for the primary analysis for the main study is based on previous studies of other agents in psoriasis patients. Based on the performance of other oral agents in recent psoriasis clinical trials, it was reasonable to assume a placebo PASI 75 response rate of approximately 10% and to plan for at least a 33% PASI 75 response rate for VB-201.

A total sample size of 150 evaluable patients (50 per group) gave 80% power to detect at the 5% significance level a difference between a placebo PASI 75 response rate of 10% and a response rate of 33% in the VB-201 group. Assuming a 17% drop out rate, a total sample size of 180 patients (60 per group) was to be randomized.

Rationale for Number of Patients in Sub-study:

Seventy-five patients were to be enrolled into the sub-study. Three dosing cohorts of 25 patients each were to be randomized in a 1:1:1 ratio to VB-201 20 mg/day, VB-201 80 mg/day or placebo. The expected percent change from baseline in the VB-201 high dose group was between 10%-15% and in the placebo group was 0%. A sample size of 60 patients, 20 in each treatment arm gave a power of at least 80%, with a significance level of 0.05 to detect this difference. Assuming a dropout rate of approximately 15% - 25%, a total sample size of 75, 25 in each treatment group, were to be randomized.

SUMMARY - RESULTS

Efficacy Results: Main study

Primary Endpoint:

For PASI 75 response rates at Week 12, the primary efficacy endpoint of the study, no significant differences from placebo were present with either VB-201 treatment group.

Secondary Endpoints:

Although no statistically significant differences from placebo were present for PASI 50 responses with either VB-201 treatment group, a higher proportion of patients treated in each VB-201 treatment group were PASI 50 responders at Week 12 compared to placebo; similarly reductions in BSA were observed in each VB-201 group at Week 12 compared to placebo.

Physician global assessment (PGA):

Based on ANCOVA analysis for the PGA, there was a decrease from baseline in PGA values for all 3 treatment groups. Compared to the placebo group change, the change for the VB-201 20 mg group was significantly (p=0.045) decreased (improved); the p-value for the VB-201 80 mg group compared to placebo was 0.15.

Using CMH, there was a statistically significant improvement in PGA in the VB-201 20 mg group compared to placebo (p=0.03), and a trend towards improvement PGA in the VB-201 80 mg group compared to placebo (p=0.12). There was a statistically significant reduction in the proportion of patients rated as “severe” (4) PGA at 12 weeks in both the VB-201 20 mg group (4.8%) compared to placebo (24.1%, p =0.003) and in the VB-201 80 mg group (6.8%%) compared to placebo (24.1% , p =0.011).

Name of Sponsor/Company: Vascular Biogenics, Ltd	**Name of Finished Product:** VB-201	**Name of Active Ingredient:** VB-201

Using logistic regression under the proportional odds model, a statistically significant improvement in PGA in VB-201 20mg compared to placebo was detected (p value=0.04, OR=2.16; CI=1.04-4.49). The same analysis for the VB-201 80 mg group showed that the effect of the 80 mg dose compared to placebo was smaller but in the same direction (OR=1.70; CI=0.81-3.56). A statistically significant effect was also detected when both 20 mg and 80 mg treatment groups were combined together and compared to placebo (p-value=0.049, OR=1.91; CI=1.00-3.65).

Patient global assessment (PtGA):

At Week 12 there was a decrease from baseline in Patient Global Assessment values for all three treatment groups. Based on ANCOVA analysis, compared to the placebo group change, this change for the VB-201 80 mg group was statistically significant (p=0.02); the p-value for the VB-201 20 mg group compared to placebo was 0.12.

Using CMH, a statistically significant improvement was observed in the 80 mg group at week 8 and week 12 when compared to placebo (p=0.02 and 0.03, respectively). Using ordered logistic regression under the proportional odds model, a statistically significant improvement in PtGA was detected in the 80mg group compared to placebo (p=0.047, OR=1.96; CI=1.01-3.80). The effect of the 20mg dose compared to placebo was smaller but in the same direction (OR=1.51; CI=0.79 -2.89).

Dose response analyses:

To assess dose-response trends, change in PASI at week 12 was analyzed by classifying VB-201 plasma levels into quartiles and evaluating the change in PASI in subjects in these quartiles. Higher plasma levels of VB-201 (higher 2 quartiles) were associated with statistically greater improvements in Total PASI score than lower plasma levels of VB-201(the lower 2 quartiles) (p=0.04). Similar findings were present for PGA (p=0.04) and PtGA (p=0.001).

Efficacy results stratified by baseline factors:

Baseline PASI score: For Week 12 PASI 50 and total PASI scores stratified by baseline PASI score, the largest difference between VB-201 treatment groups and placebo was observed in patients enrolled with PASI scores of 14.3-18.5.

Age: In sub-populations based upon age, there was a trend for higher PASI 50 response rates with VB-201 compared to placebo in the younger sub-group (≤46 years).

Baseline BSA: For PASI 50 and total PASI scores stratified by baseline BSA, the largest difference between VB-201 treatment groups and placebo was observed in patients enrolled with BSA scores of 16%-24%. In addition, for patients enrolled with BSA levels <16%, a larger decrease in PASI scores at Week 12 was noted for the VB-201 80 mg group compared to the placebo group.

Duration of psoriasis: Although no statistically significant changes were present, there was a trend for higher PASI 50 response rates among the VB-201 treatment groups compared to placebo in the 2 subsets of shorter duration psoriasis (<10 years and 10-20 years).

Prior use of systemic medications for psoriasis: At Week 12 the highest proportion of VB-201-treated patients with PASI 50 responses occurred among patients who had no previous treatment with immunosuppressants or biologicals.

Baseline high sensitivity CRP results (elevated or not elevated): Although no statistically significant changes were present, there was a trend for higher PASI 50 response rates and greater decreases in total PASI scores among the VB-201 treatment groups compared to placebo in patients with baseline CRP levels elevated. However, overall PASI 50 response rates with VB-201 treatment differed little whether the CRP level was elevated at baseline or not elevated at baseline.

Efficacy Results: PET-CT sub-study

In subjects with cardiovascular risk factors that participated in the PET-CT sub-study, 58 of the 71 patients who underwent a baseline PET-CT scan (82%) were found to have a lesion with TBR of at least 1.6 in the ascending aorta or carotid arteries, suggesting inflammation related to atherosclerosis, which qualified them for a week 12 PET. Forty-seven patients completed 12 weeks of treatment and underwent a week 12 PET-

Name of Sponsor/Company: Vascular Biogenics, Ltd	**Name of Finished Product:** VB-201	**Name of Active Ingredient:** VB-201

CT. Most patients were obese, duration of psoriasis was around 19 years, 13 patients received concomitant statins. The index vessel was defined as the ascending aorta in 39/47 (83%) of the evaluable patients.

There was a statistically significant reduction in the pre-specified measure of index vessel inflammation (most diseased segment) in the VB-201 treated patients: a 12.7% reduction from baseline in the VB-201 80 mg treatment group (p=0.04) and a 9.8% reduction from baseline in the combined VB-201 treatment groups (p=0.01). A dose-response was seen, and these reductions in vessel inflammation occurred in subjects taking concomitant statins. There was also a trend towards decrease in the mean of the maximal TBR (secondary endpoint) in the 80 mg group (-9.6%, p=0.07).

To assess correlations in dose-response, the primary endpoint of change in index vessel inflammation (most diseased segment) at week 12 was correlated to VB-201 plasma trough levels using quintiles of trough levels and evaluating the change in inflammation in subjects in these quintiles. A dose-response was seen for this endpoint: the change from baseline in the highest quintile of VB-201 plasma levels was -20.7% compared to 0.7% in the lowest 2 quintiles (p=0.047). A reduction in vessel inflammation also occurred in subjects taking concomitant statins (-18%).

Safety Results:

At a dose of either 20 mg or 80 mg/day for 12 weeks, VB-201 appeared to be safe and well-tolerated.

Two serious TEAEs were reported, neither of which was considered related to study medication or resulted in study withdrawal: a patient in the VB-201 20 mg daily treatment group with malignant melanoma in situ and a patient in the VB-201 80 mg daily treatment group who had abdominal pain resulting in a one-day hospitalization. There were no deaths in the study.

The VB-201 treatment groups had a slightly higher proportion of AEs than the placebo group: 59.2% vs. 47.5%, respectively, with very similar proportions among the two VB-201 treatment groups (20 mg: 59.1%, 80 mg 59.3%).

The most frequent AEs in the study included nasopharyngitis, diarrhea, headache, psoriasis, fatigue, rhinitis, nausea, blood CPK increased, and pruritus. Of these, nasopharyngitis, rhinitis, diarrhea, nausea, headache, and fatigue occurred more frequently in the VB-201 treatment groups than with placebo. The following AEs occurred with a frequency of at least 5% in the VB-201 treatment groups; nasopharyngitis (, diarrhea, headache, and nausea.

All AEs were classified as CTCAE Grade 1 or Grade 2 severity except for 4 Grade 3 events: the two SAEs, a patient in the VB-201 80 mg treatment group with abnormal liver function tests, and a placebo patient with back pain. Two of these Grade 3 AEs were also rated as severe: the malignant melanoma in situ and the back pain. Six patients had AEs that led to withdrawal from the study and these occurred across all three treatment groups.

No clinically significant changes in hematology, biochemistry, or lipid panel laboratory values were observed; no clinically significant trends for an increase or decrease in hematology, biochemistry, or lipid profile parameters were observed.

No clinically significant differences or trends in urinalysis testing results were found; no clinically significant differences in shifts to non-negative were observed for urinalysis testing parameters.

No clinically significant post-treatment changes in vital signs were observed, and no treatment-related changes were observed on physical exams. No clinically significant abnormalities or changes in post-treatment ECGs occurred.

Date of Report: 30 April 2012