Confidential

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Dear Dr Ajit Singh,

We have received your request for our scientific and clinical details on Metaderm and have provided them here for your information. As you know the information provided here is confidential, please therefore note to maintain confidentiality for all of the details in this document.

We at Haus Bioceuticals have developed a novel unique herbal preparation denoted Metaderm and have identified it to be a potent, safe, anti-inflammatory product with therapeutic benefit in atopic dermatitis (AD) and psoriasis. In order to develop Metaderm, we considered a number of vendors to explore material quality, compliance, and consistency measures. Biome Spagyrics met these requirements and had established good compliance measures for the ingredients that we needed to source. At Biome Spagyrics, all of the herbs that were required by Haus Bioceuticals were found to be imported from quality suppliers in countries such as United Kingdom, France and Germany. Furthermore Biome Spagyrics extraction processes did not involve any traditional knowledge or traditional processes which was one of the additional requirements for Haus Bioceuticals. Given these considerations, we sourced 4 ingredients namely A5, CE, GE, and S5 from Biome Spagyrics. Haus Bioceuticals used these to develop a proprietary mix of these ingredients into a novel topical formulation denoted as Metaderm. The scientific and clinical studies described below detail our results and findings on Metaderm.

Metaderm suppresses activated lymphocytes more significantly than azathioprine and exhibits no cytotoxicity to non-immune cells.

Azathioprine (AZA) is an immunomodulator used in the management of chronic inflammatory conditions including AD. A principal MOA of AZA is suppression of activated lymphocytes. To evaluate the immunomodulatory properties of Metaderm, we tested its capacity to suppress activated lymphocytes in comparison to AZA. In this assay $5x10^6$ lymphocytes (from unaffected controls, that have been EBV-transformed, and induced with 10µg/ml LPS) were incubated with Metaderm or AZA for 40h. Total protein levels, evaluated by SDS-PAGE, were used as measures of cell survival. As shown in Fig 2A, while AZA (100ug/ml, approximately 10 times a

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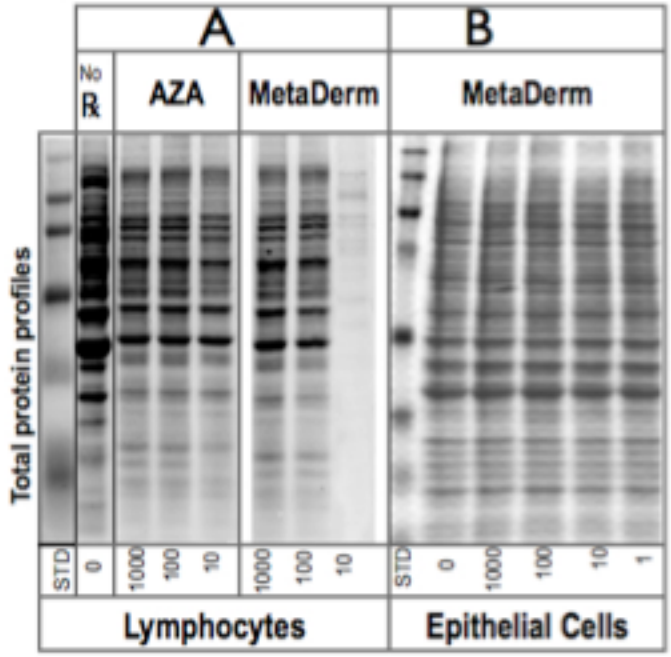
standard therapeutic dose) suppressed cell growth by ~60 % relative to untreated cultures, Metaderm (prepared as a 10% dilution of the concentrated herbal extracts in 4.9% EtOH, the same dose used in topical formulations for the clinical studies reported below) suppressed cell growth by ~90%, suggesting it has immunomodulatory properties that would be effective in AD treatment. To determine if the activated lymphocyte modulating properties of Metaderm were cell-specific, similar assays were done on several model cell lines of non-lymphoid cells, including epithelial cells and fibroblasts. We found that Metaderm exhibited no cytotoxicity in all cell types tested. Importantly, ^{1}H-NMR analyses of Metaderm showed no evidence of a corticosteroid moiety, also no changes were observed in serum cortisol levels in mice before and after oral administration, demonstrating that its immunomodulatory effects are nonsteroidal.



Metaderm exerts immunomodulatory effects through its regulation in part through TLR modulation on monocytes and keratinocytes.

The chronically relapsing immunopathogenic nature of AD has been largely attributed to increased inflammation and enhanced susceptibility to skin infections, particularly *S. aureus* that has been shown to activate the innate immune system via toll-like receptors (TLRs), resulting in pro-inflammatory gene expression and cytokine secretion in AD. To investigate the effects of Metaderm in generalized inflammation and TLR regulation, we assessed the immune response of inhibitor

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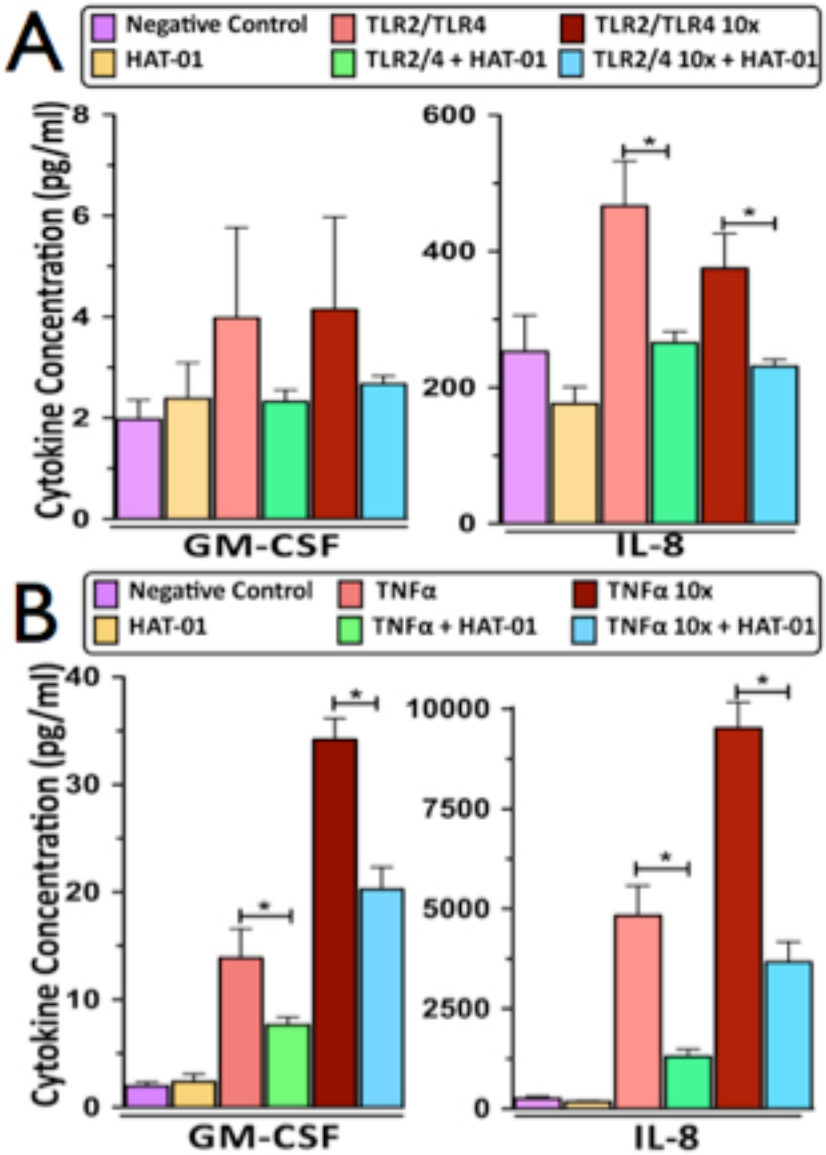
treatment following induction with several TLRs (Pam3Cys (TLR2 ligand), LPS (TLR2/TLR4 ligand), Flagellin (TLR5 ligand), FSL (TLR6 ligand), Imiquimod (TLR7 ligand)) and TNF-α on the monocytic cell line Mono Mac 6 and the human keratinocyte cell line (HaCaT). Our studies demonstrated that Metaderm down-modulated TLR2, TLR4, TLR5 and TNFα-mediated cell activation, resulting in decreased proinflammatory cytokine production, suggesting its activity is mediated, in part, via suppression of inflammatory pathways relevant to AD.



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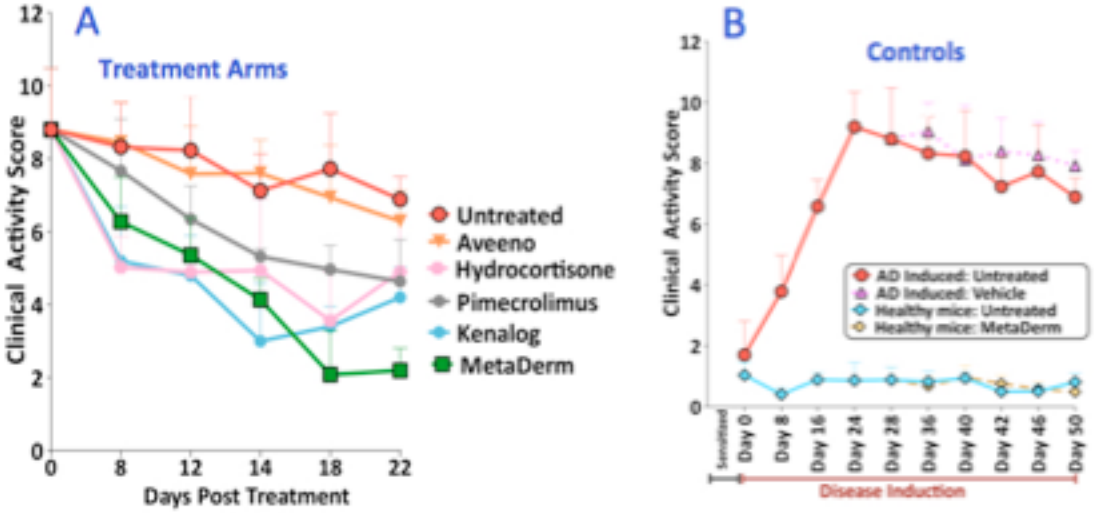
Novel therapeutic effects of Metaderm in an AD model.

Given the above results, we developed and established an AD murine model (the oxazolone-induced murine model of chronic AD) to test the therapeutic effects of Metaderm. Briefly, mice were sensitized with a single topical application of 5% oxazolone (Ox) to the flank, followed by challenges with 0.2% topical Ox every other day for total of 4 weeks. An ethanol-treated vehicle group served as an unaffectected control. Induced mice developed chronic AD as evidenced by persistent pruritic chronic dermatosis and increased epidermal hyperplasia, development of parakeratotic scales, and lymphocytic infiltrates. A dose-ranging study was performed comparing the efficacy of undiluted, 10%, 1% 0.1% herbal extract twice-daily topical applications on the site of induced-lesions was performed. The 10% extract progressively reversed the disease course as measured by a Clinical Activity Score (CAS), whereas lower dilutions had less impact. The CAS is equal to the sum of the severity of 5 signs and symptoms (itch, erythema/hemorrhage, edema, excoriation/erosion and scaling/dryness), each of which are graded on a 3-point scale (0 – none, 1 – mild, 2-moderate, 3 – severe). We also conducted a comparator-based in-vivo efficacy study in this model. Following treatment, at day 22, mean disease activity scores was decreased by 75.9% for MetaDerm treated mice relative to untreated mice. This level of efficacy was significantly higher than comparators tested: 1% pimecrolimus (p=0.002), 0.5% Kenalog (p=0.019), 1% hydrocortisone OTC (p=0.0007), and 1% Aveeno colloidal oatmeal OTC (p<0.0001). Positive effects were also observed histologically and biochemically. Skin biopsies in inhibitor-treated mice had significant decreases in hyperplasia and dermal inflammatory infiltrates relative to vehicle-treated controls (suggesting an in-vivo correlate to the in-vitro lymphocytotoxicity studies).



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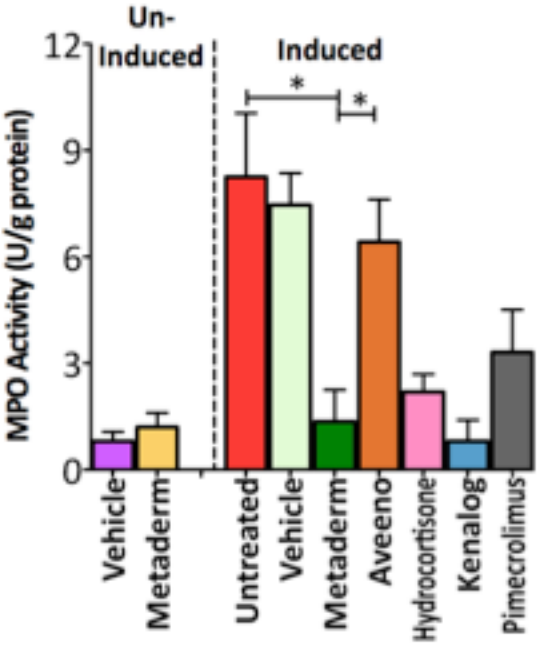
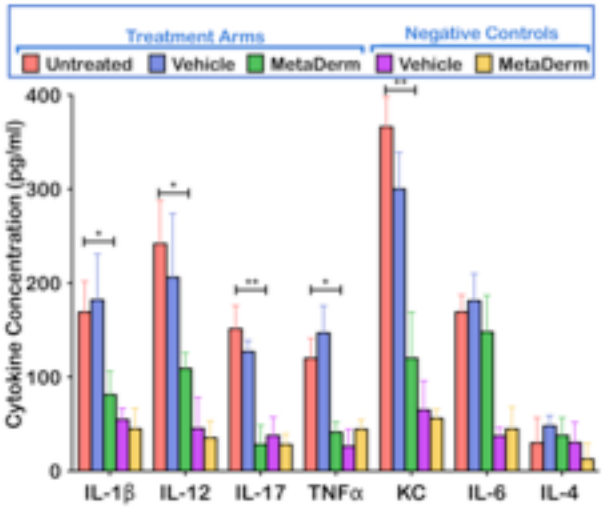
MPO Activity

Our studies also identified a mean 82.2% decrease in dermal myeloperoxidase activity, a marker of innate neutrophil infiltration, relative to vehicle and Aveeno.



Anti-inflammatory potential of Metaderm

At the systemic level, inhibitor treatment significantly decreased serum levels of the proinflammatory cytokines IL-17, IL-12, and IL-1β relative to induced vehicle-treated controls further demonstrating Metaderm's anti-inflammatory potential in AD.



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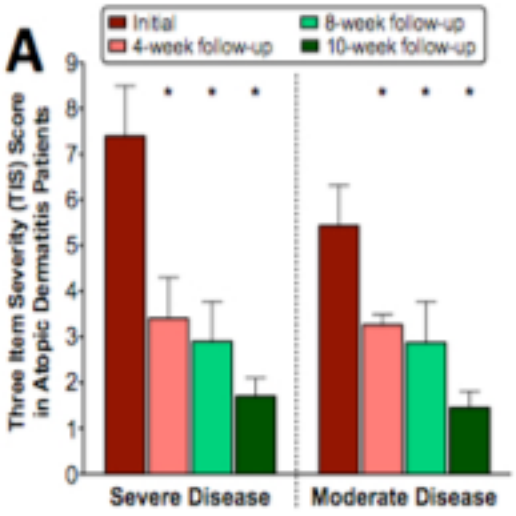
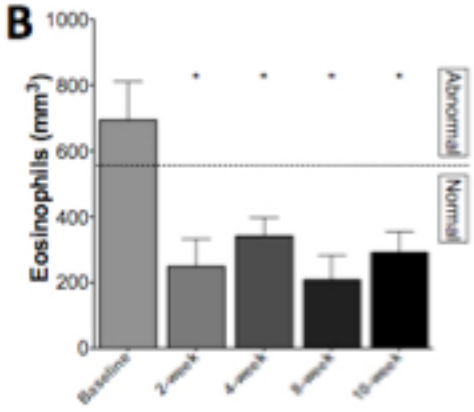
Open Label Pilot Study

To investigate the effects of Metaderm in adult AD patients, we performed an open-label clinical study with 18 patients fulfilling AD inclusion criteria. Patients were treated topically twice daily with Metaderm (300µl per lesion, prepared as a 10% dilution of the concentrated API in 4.9% EtOH) for 10 weeks. Significant resolution of symptoms and signs of AD were observed in 15 of 18 inhibitor-treated patients relative to baseline levels, and the response was sustained throughout the study (See figure below, differences in levels from initial visit with $p<0.05$, denoted with an *).



Eosinophils play an important role in modulating AD inflammation, and eosinophilia is a key AD diagnostic criterion. Peripheral blood eosinophilia was reduced in MetaDerm-treated patients at all post-baseline visits. Normal eosinophil levels were achieved after only 2 weeks, suggesting Metaderm has a rapid effect on the inflammation underlying AD.



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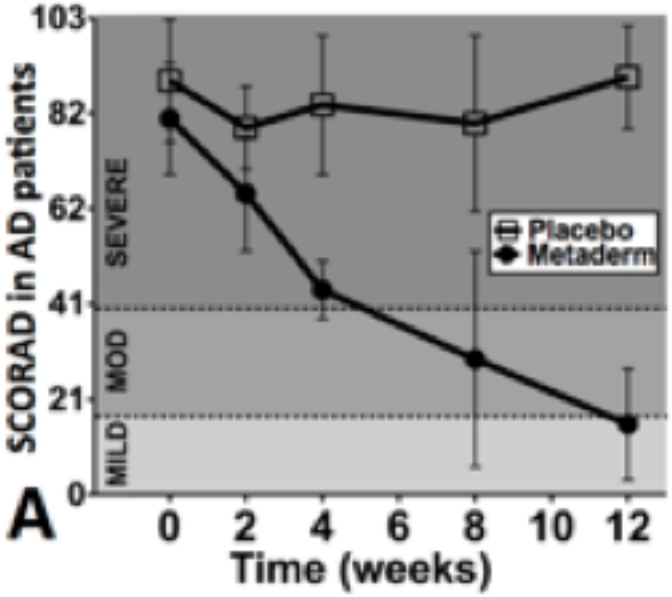
Double Blind Placebo-Controlled Study

To further investigate the safety, efficacy, and tolerability of Metaderm in adult AD, a cohort of patients fulfilling AD inclusion criteria were enrolled into a randomized double blind placebo-controlled clinical trial with a 12 week regimen of twice daily application of Metaderm (300µl per lesion, prepared as a 10% dilution of the concentrated herbal extracts in 4.9% EtOH) or vehicle.

The primary outcome was an intent-to-treat analysis of mean reduction in SCORAD (SCORAD (SCORing Atopic Dermatitis), a standardized instrument for quantifying AD severity at 12 weeks. Exploratory endpoints included interim comparisons of Metaderm vs. placebo at weeks 2, 4, 8 and 12. The trial was conducted under a multicenter protocol with three dermatology investigators. Patients were block randomized from a central location into each study arm. Patients were assessed both before and throughout the course of treatment at each visit using by SCORAD and a PGA (which assesses AD patient-relevant treatment benefit). SCORAD values, range from 0 to 103, calculated as (0.2 x Area) + (3.5 x Erythema + Edema + Crust + Excoriation + Lichenification + Dryness) + (pruritis + sleep loss). Patients are classified as mild (SCORAD <15), moderate (SCORAD 16-40) and severe (SCORAD >41).

To minimize inter-observer variability investigators received standardized training in AD clinical scoring prior to beginning the trial. Relative mean SCORAD reduction at 12 weeks between Metaderm and placebo was 69.84 units with a $p<0.0001$.



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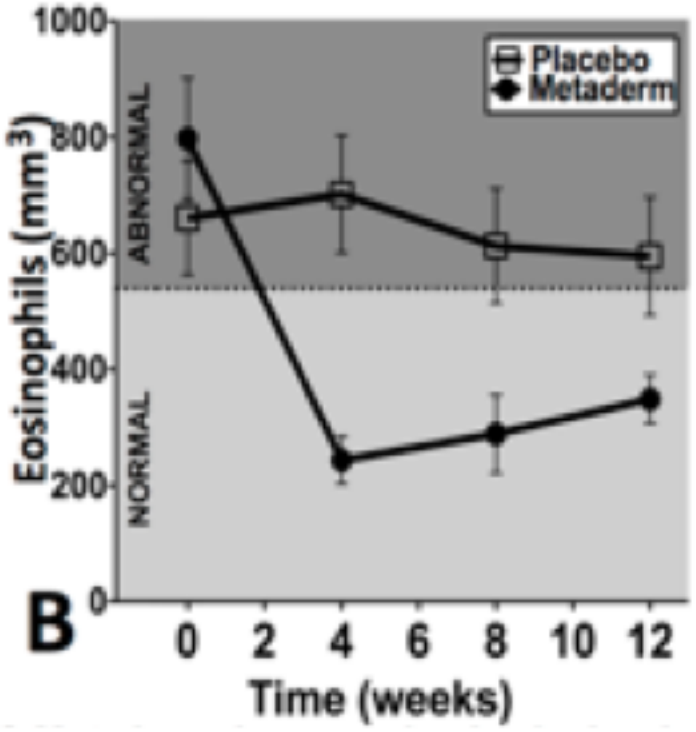
Double Blind Placebo-Controlled Study (continued)

In Metaderm-treated AD patients significant reduction in edema and erythema was observed within 4-weeks, which was followed by improvements in oozing and excoriations within 8 weeks. Significant improvement in xerosis was also observed at 4 weeks, while improvement in lichenification took up to 12 weeks for effective resolution.

Moreover, Metaderm also decreased peripheral blood eosinophilia to within normal ranges (<600 units), which did not occur in placebo.

These results further support the hypothesis that Metaderm significantly modulates AD inflammation in a clinically relevant manner. Of note, Metaderm was well tolerated, with no treatment-related adverse events observed throughout the 12-week trial.



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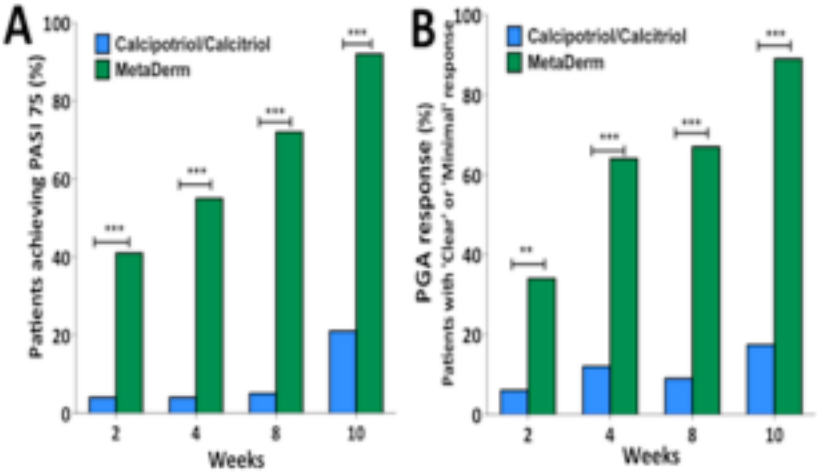
Open Label Clinical Study of Moderate to Severe Psoriasis

To investigate the effects of MetaDerm in patients with psoriasis, an exploratory 10-week open-label clinical study designed to evaluate MetaDerm efficacy and safety was conducted in adult patients with moderate to severe chronic plaque psoriasis. Patient eligibility was evaluated during a screening visit before entry into the study and was based on inclusion criteria for psoriasis, which required a psoriasis area and severity index (PASI) score ≥ 10. The clinical study had two arms: an experimental arm and a comparator arm. In the experimental arm.

Each patient was instructed to administer twice daily applications of MetaDerm. The primary endpoint for this study, analyzed on an intention-to-treat-basis, was percentage of patients obtaining an improvement in PASI greater than or equal to 75% (PASI 75) from baseline to week 10. PASI is a measure of the extent of involved skin surface area and severity of erythema, desquamation, and plaque induration (each graded on a 0–4 scale), weighted by the area of involvement into a single score in the range 0 (no disease) to 72 (maximal disease) as described. Secondary endpoints included a dynamic measure of the physician's global assessment (PGA) response, which ranges from 1 (clear) to 6 (worse) and was determined by the treating physicians. The safety of MetaDerm treatment was determined from patient reports of adverse events.

The results demonstrate a statistically significant improvement in PASI at each evaluation for the patients treated with MetaDerm. A sustained improvement in PASI was observed in the MetaDerm arm with 92% of study patients obtaining PASI 75, compared to 23% in the comparator group. Clearing of psoriatic plaques was noted as early as 2 weeks, and maximal benefit appeared at 10 weeks for the majority of patients. The PGA scores correlated with the PASI 75 in that they were



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significantly better in the patients receiving MetaDerm versus the comparator. In all, 89% of patients achieved a "clear" or "minimal" PGA response when compared to 17% from the comparator group.

Improvement across all symptoms (itching, irritation, sensitivity, bleeding, and scaling) in both frequency and severity was observed, and differences between absolute improvements were similar for most symptoms.

MetaDerm was well tolerated, with no treatment-related adverse events observed throughout the 10-week trial. In contrast at 10 weeks of treatment, 4 patients that were treated with topical calcipotriol exhibited local treatment-site irritation and burning sensation. These findings further support the hypothesis that MetaDerm significantly reduced the disease activity of psoriasis in a clinically relevant manner.

The above details comprise all our findings on Metaderm.

Sincerely,

Michael Centola, Ph.D.
Chief Executive Officer
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