

# Key Events

## Dermatology

*Last Updated: 22<sup>nd</sup> February 2007*

Date	Event
February 2-6, 2007	65 <sup>th</sup> Annual Meeting of the American Academy of Dermatology

### Executive Summary

Earlier this month, medical professionals from all over the world gathered for the American Academy of Dermatology's (AAD) 65th Annual Meeting. In Wood Mackenzie's view, the key messages were:

- Developments in the treatment of psoriasis represented a key area of interest.
- The potential for increased use of biologics for patients with severe psoriasis was highlighted as physicians become more comfortable with these therapies. However, physicians remain uncertain about treatment choice given inconclusive evidence on differences in efficacy among treatments, and a lack of head-to-head data. This would suggest an opportunity for any company prepared to make the necessary investment in relevant clinical studies.
- The potential for biologics in the management of psoriasis may be tempered by their high expense, particularly in cost-restrictive markets.
- Positive Phase III clinical trial results for Abbott/ CAT's **Humira** in the REVEAL trial will lead to 2007 US and EU filing. UCB's **Cimzia** will likely advance to Phase III following positive Phase II safety and efficacy data.
- Absence of novel treatments in pipeline for the treatment of acne, rosacea, and atopic dermatitis. New delivery systems and formulations rule innovation.

### Key Prescribing Messages

#### Psoriasis

Treatment paradigms for psoriasis are changing. Currently, in the majority of cases, traditional methods of treatment like topical steroids are used as first-line therapy, particularly in patients with mild psoriasis. However, physicians are starting to welcome the idea of newer biologics for treatment of patients with severe psoriasis. With **Amevive**, **Enbrel**, and **Raptiva** on the market since 2004, **Remicade** now available (approved in the US in late 2006), and **Humira** (expected in 2008) and **Cimzia** on the horizon, the rapidly expanding market is becoming overwhelming as physicians try to sort out their options.

As more clinical data becomes available to support the short and long term efficacy of these biologic therapies, we believe that many physicians will become more comfortable prescribing them among larger patient populations. Using the analogy of anti-TNFs in the rheumatoid arthritis (RA) market, physicians gradually became more comfortable prescribing biologic medications early on as a first-line therapy to prevent the progression of the disease and allow patients to enter remission. In Wood Mackenzie's opinion, the prescribing habits of many dermatologists will follow this trend, allowing biologics to gradually earn a greater share of the psoriasis market.

According to an estimate by Amgen, as of late 2006 biologic penetration of moderate to severe psoriasis patients was 6%. Considering that this market is still relatively new, we expect this figure to continue to increase. However, the high expense of the treatments may temper penetration in cost-restrictive markets, particularly in the EU.

#### Acne

In the area of acne, there currently aren't many novel treatments in the pipeline. Alternate formulations for existing treatments seem to be the current trend. Alan R. Shalita, M.D., Professor and Chairperson of the Department of Dermatology at Down State Medical Center, SUNY highlighted what he expects to see in the future including new combinations, new antibiotics, retinoids, peptides, and ALA-PDT (5-amino-levulinic acid and photodynamic therapy).

Given the current absence of any billion dollar acne drug due to the wide variety of treatments currently available and new mechanisms of action still in discovery, many Big Pharma companies are not investing in acne therapies. Witness Pfizer's recent exit from R&D funding in any new dermatology treatments – other companies may follow suit or continue to focus their development resources toward more lucrative areas of research like biologics for psoriasis treatment.

In women, the use of certain oral contraceptives was highlighted for the treatment of acne. In late January 2007, Bayer-Schering's **Yaz**, (drospirenone and ethinyl estradiol) became the third oral contraceptive to receive an acne indication from the FDA (following J&J's **OrthoTricyclen** and Bayer-Schering's **Yasmin**).

### Rosacea

Similar to the acne market, new treatments of rosacea include re-formulations of existing treatments. For example, CollaGenex's **Oracea** (doxycycline) is a re-formulated oral tetracycline that offers anti-inflammatory properties, but has little anti-bacterial properties. While this drug has the benefit of an antibiotic resistance profile similar to placebo, it will have to compete against widely used generics.

### Atopic Dermatitis

Similar to acne and rosacea, there aren't many novel drugs in the pipeline for the treatment of atopic dermatitis. Many innovators are focused on combinations and different delivery methods (ointment vs. gel vs. foam, etc.) of topical steroids. Products of interest include Galderma's **Clobex** spray (clobetasol propionate) and Stiefel Laboratories' **Verdeso** (desonide foam), which are essentially new formulations of older treatments. While these new products offer some minor benefits of convenience and improved efficacy, many physicians are concerned about the cost of these new combination therapies and may continue to prescribe cheaper generic formulations of the drugs.

## Key Clinical Data

### Meta-analysis of biologic treatments for psoriasis

With many biological therapies now available for the treatment of moderate to severe psoriasis and little head-to-head data, many physicians are trying to sort out existing clinical information to weigh and compare relative safety and efficacy levels among these treatments. Treatments of interest included J&J/ Schering-Plough's **Remicade** (infliximab), Abbott/ CAT's **Humira** (adalimumab), Amgen/Wyeth's **Enbrel** (etanercept), Genentech/ Merck Serono's **Raptiva** (efalizumab), and Astellas' **Amevive** (alefacept).

While there is no conclusive evidence to support the superior efficacy of one treatment over the other, Mark Bechtel, M.D., Director of Dermatology at The Ohio State University College of Medicine spoke on a meta-analysis of existing clinical information to compare the efficacy of these treatments in severe psoriasis. It was highlighted that several of the studies may have varied patient demographics, time frames for evaluation of efficacy endpoints, and onset of action which make them difficult to compare across the board. However, as all patients were objectively scored they were able to compare the percentage of patients achieving PASI (Psoriasis Area and Severity Index) 75 across clinical studies at two time-points (10-12 weeks and 24-26 weeks).

	% of patients achieving PASI 75 at 10-12 weeks	% of patients achieving PASI 75 at 24-26 weeks
Remicade	76-88	78-82
Humira (40 mg/wk)	80	77
Humira (40 mg/eow)	53-77	67
Enbrel (50mg 2x/wk)	46	50
Raptiva	22-41	44
Amevive	21	33

Table 1. Mark Bechtel, M.D. 65<sup>th</sup> Annual Meeting of the American Academy of Dermatology.

The results in Table 1 show that patients treated with **Remicade** and **Humira** (weekly) were most effective, displaying rapid response rates with 76-88% and 80% of patients achieving a PASI 75 at 10-12 weeks, respectively. Data also showed that there was no significant improvement in patients taking these treatments for a longer period of time 24-26 weeks.

Although these results aren't conclusive, they do show that there are differences in efficacy among the biologics in the treatment of psoriasis, which are not seen in other indications, such as rheumatoid arthritis. With **Remicade** now available for psoriasis in the US since September 2006 and **Humira** expected to be on the market by 2008, further clinical studies including a head-to-head trial proving this potentially superior efficacy could help boost the market penetration of these products to effectively compete against the current leader **Enbrel**.

## Key Clinical Trial Results

### Psoriasis

- Abbott presented results from the REVEAL (Randomized Controlled Evaluation of Adalimumab Every Other Week in Dosing Moderate to Severe Psoriasis Trial) trial, a pivotal Phase III study evaluating **Humira** (adalimumab) in adult patients with moderate to severe chronic plaque psoriasis. Results showed that treatment with 40mg of **Humira** every other week is efficacious for patients with moderate to severe psoriasis. Abbott will submit results from this trial and the CHAMPION (Comparative Study of Humira vs. Methotrexate vs. Placebo in Psoriasis Patients) study as part of a regulatory application for a psoriasis indication in the US and EU during the first half of 2007. Approval and market entry is expected in 2008.

- UCB presented results from a Phase II trial to evaluating the efficacy and safety of **Cimzia** (certolizumab pegol) in patients with chronic plaque psoriasis. Results showed that **Cimzia** demonstrated statistically significant efficacy over placebo and was well-tolerated among patients. As a result of this study, we expect the product to enter into Phase III clinical studies in mid-2007.

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