# PIPELINE PREVIEWS

Pipeline Previews brings to you information on the newest drugs and medical products as they become available to the dermatologic community. This department may include additional information from the manufacturers, plus reports from physicians who wish to share their clinical experience with these new products. In addition, we will inform our readers about the latest drugs receiving Food and Drug Administration (FDA) approval.

## FDA Approves Cosentyx for Psoriasis

Novartis has announced that the FDA has approved Cosentyx for the treatment of moderate-to-severe plaque psoriasis in adult patients who require systemic therapy or phototherapy (light therapy). According to Novartis, Cosentyx is the first approved human monoclonal antibody that selectively binds to interleukin IL-17A.

The FDA approval was based on the positive efficacy and safety outcomes from 10 phase II and phase III studies which included over 3,990 adult patients with moderate-to-severe plaque psoriasis. The Phase III clinical program included four placebo-controlled studies which examined Cosentyx 300 mg and 150 mg in patients with moderate-to-severe plaque psoriasis. In these studies, Cosentyx met all primary and key secondary endpoints, including Psoriasis Area and Severity Index (PASI) 75 and 90 and Investigator's Global Assessment modified 2011 (IGA) 0/1 responses, showing significant skin clearance at week 12. Cosentyx (300 mg) also maintained its safety profile when compared to Enbrel (etanercept) and Stelara (ustekinumab).

Cosentyx was also recently approved in the EU for the treatment of moderate-to-severe plaque psoriasis in adult patients who require systemic therapy or phototherapy (light therapy. Cosentyx had previously been approved in Australia for the treatment of moderate-to-severe plaque psoriasis and in Japan for the treatment of moderate-to-severe plaque psoriasis and active psoriatic arthritis.

Novartis reports that it is also evaluating Cosentyx for the treatment of ankylosing spondylitis and psoriatic arthritis. Regulatory applications for these indications are scheduled in 2015.

Novartis announces FDA approval for first IL-17A antagonist Cosentyx(TM) (secukinumab) for moderate-to-severe plaque psoriasis patients.

Offering a new treatment option for patients, Cosentyx is the first approved human monoclonal antibody (mAb) that selectively binds to interleukin IL-17A.

Phase III data demonstrated Cosentyx resulted in clear or almost clear skin in the majority of patients with moderate-to-severe plaque psoriasis

## Cobimetinib and Zelboraf (Vemurafenib) in Advanced Melanoma

Genentech has announced that the FDA has accepted and granted Priority Review for the company's New Drug Application (NDA) for cobimetinib in combination with Zelboraf® (vemurafenib) for the treatment of people with BRAF V600 mutation-positive advanced melanoma. The FDA will make a decision on approval by August 11, 2015.

The NDA is based on results of the coBRIM Phase III study, which showed the MEK inhibitor cobimetinib plus Zelboraf reduced the risk of disease worsening or death by half in people who received the combination (hazard ratio [HR]=0.51, 95 percent confidence interval [CI] 0.39-0.68; $p<0.0001$), with a median PFS of 9.9 months for cobimetinib plus Zelboraf compared to 6.2 months with Zelboraf alone. The safety profile was consistent with a previous study of the combination. The most common Grade 3 or higher adverse events in the combination arm included liver lab value abnormalities, elevated creatine phosphokinase (CPK, an enzyme released by muscles) and diarrhea. The most common adverse events seen in the combination arm included diarrhea, nausea, rash, photosensitivity and lab value abnormalities.

The coBRIM study is an international, randomized, double-blind, placebo-controlled Phase III study evaluating the safety and efficacy of 60 mg once daily of cobimetinib in combination with 960 mg twice daily of Zelboraf, compared to 960 mg twice daily of Zelboraf alone. In the study, 495 patients with BRAF V600 mutation-positive unresectable locally advanced or metastatic melanoma (detected by the cobas® 4800 BRAF Mutation Test) and previously untreated for advanced disease were randomized to receive Zelboraf every day on a 28-day cycle plus either cobimetinib or placebo on days 1-21. Treatment was continued until disease progression, unacceptable toxicity or withdrawal of consent. Investigator-assessed PFS was the primary endpoint. Secondary endpoints include PFS by independent review committee, overall response rate, overall survival, duration of response and other safety, pharmacokinetic and quality of life measures.

There was a higher overall frequency of Grade 3 or higher adverse events in the combination arm (65 vs. 59 percent), with close to half of these due to lab value abnormalities (mainly increased blood levels of liver enzymes and CPK). Common adverse events (occurring in more than 20 percent) observed at a

higher frequency (all grades) in the combination arm compared to the Zelboraf arm included diarrhea (57 vs. 28 percent), nausea (39 vs. 24 percent), photosensitivity (28 vs. 16 percent), lab value abnormalities (increased alanine aminotransferase [ALT, 24 vs. 18 percent], increased aspartate aminotransferase [AST, 22 vs. 13 percent], increased CPK [30 vs. 3 percent]) and vomiting (21 vs. 12 percent). Common adverse events observed at a lower frequency in the combination arm included hair loss (14 vs. 29 percent), thickening of the outer layer of the skin (10 vs. 29 percent) and joint pain (33 vs. 40 percent). Most instances of each common adverse event were Grade 1 or 2 in severity.

Other select adverse events that were lower in the combination arm included cutaneous squamous cell carcinomas (3 vs. 11 percent; all grades) and keratoacanthomas (<1 vs. 8 percent; all grades). Serous retinopathy (collection of fluid under the retina) was observed at a higher frequency in the combination arm (20 vs. <1 percent) with most of these events either Grade 1 or 2 and temporary in nature. Specific adverse events leading to withdrawal from treatment were similar in both study arms, as was the overall discontinuation rate from treatment (13 vs. 12 percent).

## Soligenix and Cutaneous T-Cell Lymphoma

Soligenix, Inc. has announced that its SGX301 (synthetic hypericin) development program for the first-line treatment of cutaneous T-cell lymphoma (CTCL) has received "Fast Track" designation from the FDA.

Fast track is a designation that the FDA reserves for a drug intended to treat a serious or life-threatening condition and one that demonstrates the potential to address an unmet medical need for the condition. Fast track designation is designed to facilitate the development and expedite the review of new drugs. For instance, should events warrant, Soligenix will be eligible to submit a new drug application (NDA) for SGX301 on a rolling basis, permitting the FDA to review sections of the NDA prior to receiving the complete submission. Additionally, NDAs for fast track development programs ordinarily will be eligible for priority review, which imparts an abbreviated review time of approximately six months.

SGX301 is a novel first-in-class photodynamic therapy utilizing safe visible light for activation. The active ingredient in SGX301 is synthetic hypericin, a potent photosensitizer which is topically applied to skin lesions and then activated by fluorescent light 16 to 24 hours later. Combined with photoactivation, hypericin has demonstrated significant anti-proliferative effects on activated normal human lymphoid cells and inhibited growth of malignant T-cells isolated from CTCL patients. In a published Phase 2 clinical study in CTCL, patients experienced a statistically significant ($p < 0.04$) improvement with topical hypericin treatment whereas the placebo was ineffective: 58.3% compared to 8.3%, respectively. SGX301 has received orphan drug designation from the FDA.

## FDA Approves VenaSeal Closure System

The FDA has approved the VenaSeal closure system to permanently treat varicose veins of the legs by sealing the affected superficial veins using an adhesive agent.

The VenaSeal system is intended for patients with superficial varicose veins of the legs that cause symptoms. The sterile kit is made up of an adhesive, a specially formulated n-butyl-2-cyanoacrylate, and delivery system components that include a catheter, guidewire, dispenser gun, dispenser tips, and syringes.

The device must be used as a system and differs from procedures that use drugs, laser, radio waves or cuts in the skin to close or remove veins. A trained healthcare professional inserts the catheter through the skin into the diseased vein to allow injection of the VenaSeal adhesive, a clear liquid that polymerizes into solid material. The healthcare professional monitors proper placement of the catheter using ultrasound imaging during delivery of the adhesive into the diseased vein to seal it. The FDA reports that because the VenaSeal system does not incorporate heat application or cutting, the in-office procedure can allow patients to quickly return to their normal activities, with less bruising.

The FDA reviewed data for the VenaSeal system in a premarket approval application, the agency's pathway to evaluate safety and effectiveness of Class III medical devices. Data supporting the FDA approval included results from three clinical studies sponsored by the manufacturer. The U.S. clinical study assessed the safety and effectiveness of the VenaSeal system in 108 participants compared to radio-frequency ablation in 114 participants. The trials showed the device to be safe and effective for vein closure for the treatment of symptomatic superficial varicose veins of the legs.

The VenaSeal system should not be used in patients who have a known hypersensitivity to the VenaSeal adhesive, acute inflammation of the veins due to blood clots or acute whole-body infection. Adverse events observed in the trial—and generally associated with treatments of this condition—included vein inflammation (phlebitis) and burning or tingling (paresthesia) in the treatment zone.

## Restylane® Silk for Lip Enhancement and Perioral Lines

Galderma has announced the launch of Restylane® Silk, the first and only dermal filler approved by the FDA for lip enhancement and the treatment of wrinkles and lines around the mouth in people over the age of 21. Restylane® Silk is a smooth gel designed to restore natural youthful definition and symmetry to the lip and mouth area.

In a clinical study involving 221 patients, investigators observed that 77% of patients treated with Restylane® Silk showed an improvement in lip fullness 8 weeks after treatment and 59% of treated patients maintained lip fullness six months after treatment.

In the same study, 98% of patients treated with Restylane® Silk reported a visible improvement in the fullness of their lips 14 days after injection and 76% reported that they still had lip improvement at six months following injection.

Restylane® Silk is administered by a physician or qualified healthcare professional. The product is injected into a patient's lip and/or area around the mouth in one or two sessions as needed and the process typically takes less than one hour. In the clinical study, the results of Restylane® Silk lasted approximately 6 months following treatment. The most common side effects observed following treatment with Restylane® Silk were: swelling, tenderness, bruising, pain and redness. The majority of these side effects were mild and decreased in severity within 2-7 days. These side effects have also been observed in other lip enhancement clinical trials.

Treatment volume should be limited to 1.5 mL per lip per treatment and 1.0 mL for perioral rhytid correction, as greater amounts significantly increase moderate and severe injection site reactions.

## L'Oréal International Awards for Social Responsibility in Dermatology New Closing Date - April 15th 2015

L'Oréal announced today the extension of the closing date of its International Awards for Social Responsibility in Dermatology to April 15th 2015.

Patients with dermatological conditions may frequently face discrimination and feel socially excluded, even children. The International Awards for Social Responsibility in Dermatology, "Caring to Inspire Skin Confidence" aim to acknowledge and celebrate the often unseen efforts and hard work carried out by dermatologists worldwide: all their voluntary dermatological initiatives that improve patients' physical and psychological health and self-esteem, independently from their medical treatment.

L'Oréal created an independent Steering Committee of 7 worldwide renowned dermatologists, who will evaluate each initiative and select five winners, one per major geographical zone: Asia-Pacific, Africa and the Middle East, Europe, North America, and Central-South America.

These awards are supported by the International League of Dermatological Societies (ILDS) and by the 23rd World Congress of Dermatology and the Awards Ceremony will be held at the 23rd World Congress of Dermatology in Vancouver, Canada, on June 9, 2015.

## First Derm Dermatology Q&A App Tops 100,000 Downloads

First Derm, a dermatology question-and-answer app that is available in the Apple AppStore and Google Play Store, has reached 100,000 downloads.

The app launched a little more than a year ago: January 2014.

First Derm allows users to anonymously take pictures of external skin problems and send them to a licensed dermatologist, who will respond to inquiries within 24 hours of receiving the pictures with an assessment of the problem. App users are asked to send two pictures — one close up and another farther away — along with a description of the skin condition. The consultation costs $40 for each case submitted for assessment.

Users do not have to make an account or register to use the app. First Derm aims to keep all user information anonymous. Another addition to the app is its geo-location abilities that allow a user to locate the nearest pediatrician, dermatologist or pharmacy.

"The main focus is to triage the right patient at the right time to the right level of healthcare," Alexander Borve, the CEO of First Derm parent company iDoc24, told MobiHealthNews when the app launched last year. "We have an international network of dermatologists, working in five different languages. They have been vetted by our advisory board. Around 20 percent of cases are audited every month to keep a high standard."

## FDA Panel Backs Non-Surgical ATX-101 by Kythera for Double-Chin Treatment

Kythera Biopharmaceuticals Inc. said that the Food and Drug Admnistration advisory panel voted unanimously to recommend approval of the company's injectable drug ATX-101 to treat adult submental fat, or what is commonly known as a double chin.

The treatment would be a nonsurgical option for double chin, which the company calls a much-cited but undertreated aesthetic complaint that results in an older and heavier facial appearance.

## A New Council Has Been Formed to Rid the World's Operating Environments from Surgical Plume

A new non-profit council has recently formed with a mission to finally rid the world's operating environments of surgical smoke plume once and for all. With the participation of key clinical stakeholders, clinician based organizations, industry partners, and standard setting bodies, this new consensus body is known as the International Council on Surgical Plume (ICSP). The charter of this Council is to provide education, aid in the creation of new clinical studies, drive regulatory reform, and advocate enforcement of existing mandates related to surgical plume throughout the world.

With the formation of the ICSP, surgical stakeholders can join in one voice to advocate for clearer mandates, better dissemination of existing studies, construct meaningful new studies that resonate with those not yet advocating for plume management, and review of new and existing clinical information for scientific credibility.

Individual clinicians, clinical organizations, educators, safety advocates, standard setting bodies, and other surgical team members are encouraged to join in this effort to rid surgical environments of the hazards associated with plume inhalation.

### Buffalo Filter Launches LaparoVue™ Visibility System

Buffalo Filter is pleased to announce LaparoVue™ Visibility System our newest entry into the laparoscopic market. Understanding a surgeon's need to see clearly during laparoscopic surgery, LaparoVue is an all-in-one solution designed to take the complexity out of achieving optimal visualization. An easy to use, disposable multi-purpose device that warms, white balances, cleans and defogs, LaparoVue eliminates the necessity for multiple product purchases.

### TRIANEX® 0.05%(Triamcinolone Acetonide Ointment,USP) Now Available from Promius Pharma, LLC

Promius Pharma, LLC, has acquired the rights to market and distribute Trianex® 0.05% (Triamcinolone Acetonide Ointment, USP) in the United States from CMP Pharma, Inc. Trianex Ointment, a mid-potency corticosteroid, is notable for its white formulation that has the look and feel of a cream.

Trianex Ointment will be available in a 430 gram jar and features a proprietary cream-like formulation. It will be the only ointment to offer this combination, making it an appealing option for those patients with inflammatory skin conditions that cover large areas and who don't like the typical greasy feel of ointments.

### Provectus Biopharmaceuticals Awarded PH-10 Patent by U.S. Patent and Trademark Office

Provectus Biopharmaceuticals, Inc. announced that it has received U.S. Patent No. 8,974,363 from the United States Patent and Trademark Office (USPTO). The new patent, entitled "Topical medicaments and methods for photodynamic treatment of disease," provides detailed protection of the Company's investigational dermatological drug PH-10.

Provectus Biopharmaceuticals, Inc., specializes in developing oncology and dermatology therapies. PV-10, its novel investigational drug for cancer, is designed for injection into solid tumors (intralesional administration), thereby reducing potential for systemic side effects. Its oncology focus is on melanoma, breast cancer and cancers of the liver. The Company has received orphan drug designations from the FDA for its melanoma and hepatocellular carcinoma indications. PH-10, its topical investigational drug for dermatology, is undergoing clinical testing for psoriasis and atopic dermatitis.