

INDUSTRY CONSOLIDATION CONTINUES, VALEANT/MEDICIS DEAL COMPLETE

Valeant Pharmaceuticals acquired Medicis Pharmaceutical for \$44 per share in cash in December, in a deal worth approximately \$2.6 billion. The combined operations will be located in Scottsdale, AZ, and will operate under the name Medicis.

Medicis' portfolio of aesthetic and dermatologic drugs includes Solodyn (Minocycline HCl Extended Release Tablets), the Restylane family of injectable fillers, the Perlane family of injectable fillers, Dysport (abobotulinumtoxinA), and Zyclara (imiquimod). Valeant reports that the company plans to have roughly 350 sales representatives in the US, targeting prescription dermatology, aesthetics, and podiatry.

Immediately upon the closing, Valeant implemented plans to cut \$225 million in costs, slashing more than 300 jobs in redundant departments. According to Reuters, Valeant CEO J. Michael Pearson predicated in an analyst call that revenue would hit up to \$4.8 billion in 2013 (up from an expected \$3.4 to \$3.6 billion in 2012).

At the 2012 Cosmetic Surgery Forum (CSF) in Las Vegas in December, former CEO of Medicis Jonah Shacknai spoke about the pending acquisition and expressed gratitude for his many years in the dermatology industry. He stressed his confidence in the new leadership at Medicis and Valeant. On receiving the Lifetime Achievement Award in Dermatology at CSF, Mr. Shacknai observed that he expects new leadership at Valeant to bring greater customer-centricity to the company as it continues to grow and serve the specialties it targets. "Valeant is now the



largest dermatology company in the world, and with that kind of stature comes a whole lot of responsibility," said Mr. Shacknai.

The company's dermatology R&D operations will be located in Laval, Quebec, Scottsdale, AZ, and Petaluma, CA, and corporate support functions will be based in New Jersey.

In other acquisition news, Allergan, Inc. completed the acquisition of SkinMedica, Inc. Under terms of the agreement, which was first announced on November 16, 2012, Allergan paid approximately \$350 million (subject to certain adjustments) for the business, best known for marketing a variety of physician dispensed non-prescription aesthetic skin care products and prescription products. Allergan plans to operate SkinMedica as a separate global business based out of SkinMedica's current headquarters in Carlsbad, CA.

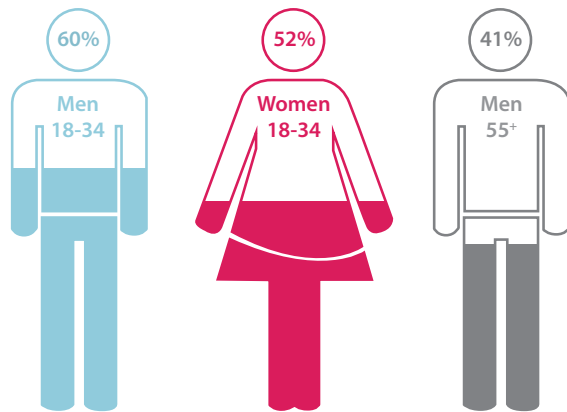
Belotero Now Available Nationwide

Belotero Balance is now available nationwide from Merz Aesthetics for the correction of moderate-to-severe facial wrinkles and folds. This dermal filler joins the Merz Aesthetics portfolio of injectable products, which includes Radiesse Volumizing Filler and Asclera (polidocanol) Injection. The FDA approved Belotero Balance based on the results from a randomized, double-blind, active-controlled, multicenter study of 118 patients. In a split-

face design, patients received bilateral treatment with the product and an approved bovine collagen filler for the correction of moderate-to-severe nasolabial folds. Treatment with Belotero Balance resulted in a decrease in the severity of the folds from baseline, according to the company.



Online “Beauty Product” Sales



New research shows that while buying beauty products has become mainstream for men, those age 18-34 agree that buying online is more convenient than shopping in-store. This compares to 52% of women of the same age and 41% of older men, research firm Mintel reports.

In-office dispensers, take note: 43% of men who shop online said it gives them early access to new products, while 73% think it saves them time. Consumers are hungry for product guidance. About half of men and women said they would use apps to guide product selection. Roughly half of men and a third of women wanted interactive features like live chat to aid online shopping.

New Fractionated Skin Resurfacing Module Enhances RF Laser Treatments

The PixelRF fractionated skin resurfacing module from Alma Lasers, Inc. uses proprietary InMotion Refractive Radiofrequency Micro Plasma Technology, which both ablates and heats the skin through controlled, focused delivery of energy without using disposables. The PixelRF was recently added to Alma’s Accent family of products, and it can achieve in as little as one session what would require multiple sessions with other RF technologies, according to the company. It works by causing evaporation, mechanical damage, and thermal damage deep beneath the epidermis surface, providing significant dermal impact with minimal epidermal disruption. Patients are recommended to undergo one to four PixelRF treatments, administered every four weeks. Optimal results are typically seen in two to three months.

FDA Approves Pliaglis Novel Topical Anesthetic

Nuvo Research’s Pliaglis (lidocaine & tetracaine) Cream 7%/7% topical anesthetic cream, designed to minimize

can be safely administered to multiple patients and, after reconstitution, can be stored beyond the recommended time period of four hours, according to a new study. Investigators examined current clinical practices and expert consensus recommendations regarding the reconstitution and storage of botulinum toxins and conducted an Internet-based study to analyze current practices of members of the ASDS administering botulinum toxins.

After product reconstitution, the majority of physicians (68.6 percent) routinely store botulinum toxin for a period of greater than one week and safely use each toxin vial for more than one patient. Not a single case of infection was observed. However, the authors noted that this was a single survey with a 32.2 percent response rate.

—*J Am Acad Dermatol*; 67(3): 373-8

FULL-FACE REJUVENATION WITH FILLERS SHOWN EFFECTIVE

Full-face rejuvenation using a range of hyaluronic fillers can offer safe, effective results, as well as notable patient satisfaction, new findings indicate. In a six-month study, participants

SURGEONS DIFFER ON ETHICS OF RHINOPLASTY

Aesthetic rhinoplasty surgeons appear to have diverging opinions about the ethical issues they may face in practice. A recent survey of the opinions, practices, and attitudes of experienced and novice facial plastic surgeons presented 15 clinical vignettes addressing ethical quandaries in aesthetic rhinoplasty and based on the experience and observations of the senior author over nearly 30 years of practice and teaching. Five of the 15 vignettes demonstrated significant differences between the responses of the fellowship directors and the fellows, and no single vignette had a unanimous consensus in either group. The survey was fielded anonymously to Fellowship directors and facial plastic surgery fellows of the American Academy of Facial Plastic and Reconstructive Surgery.

— *Arch Facial Plast Surg*. 2012

SAFE STORAGE TIMES FOR BOTULINUM TOXINS LONGER THAN THOUGHT

Assuming standard safe injection techniques are followed, a single vial of onabotulinumtoxinA (BT-A)

The Annual Plastic Surgery Pricing Report for 2013 from BuildMyBod (<http://www.buildmybod.com>) highlights complete procedural costs from Board Certified Plastic Surgeons around the United States including member-surgeons of the American Society of Plastic Surgeons (ASPS) and The American Society for Aesthetic Plastic Surgery (ASAPS).

According to Google search data, 10% of the millions of Google searches that occur monthly within the plastic surgery space, are explicitly seeking procedure pricing and cost information.

pain during aesthetic dermatological procedures such as dermal filler injection, pulsed dye laser therapy, facial laser resurfacing, and laser-assisted tattoo removal, now has FDA approval. Galderma has partnered with Nuvo to market the product. The approval comes on the heels of a Complete Response Letter issued by the FDA earlier this year, which raised issues that Nuvo and Galderma (its partner on Pliaglis) have successfully addressed. Pliaglis uses Nuvo's proprietary phase-changing technology to form a pliable peel on the skin when exposed to air. Earlier this year, Galderma stated that several European countries have approved Pliaglis, suggesting a global launch of the product is imminent.

could receive five different fillers from the same range (HA(E)) for up to eight indications (periorbital lines, tear troughs, cheeks, cheek folds, nasolabial folds, upper lip lines, lips, and marionette lines). Outcomes included global aesthetic improvement scores, improvement in each indication, adverse events, local tolerability, and satisfaction.

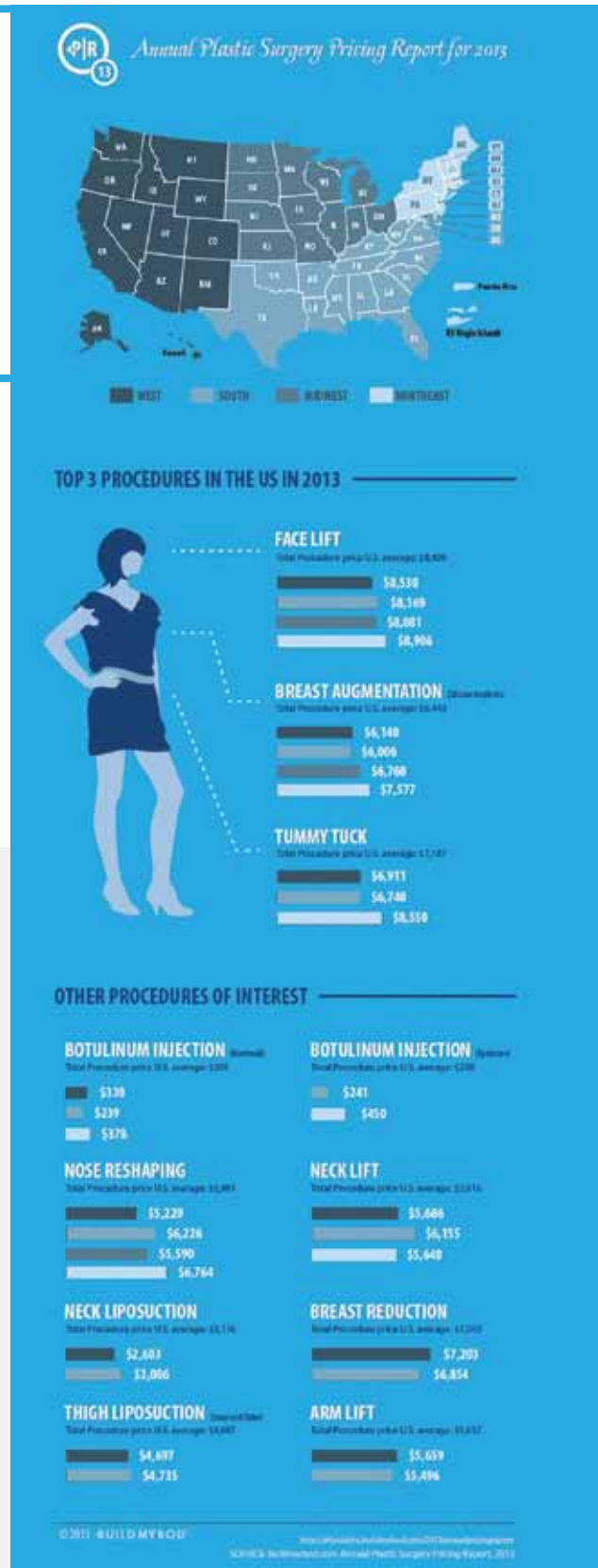
A total of 77 participants with a mean age of 54.5 were enrolled; 48.1 percent had five or more indications treated. Mean total injection volume (baseline and touch-up) per participant was 6.7mL. **At six months, 92.1 percent of participants remained at least improved over baseline, 79.7 percent of participants were satisfied or very satisfied with the durability of results, and 63 percent of participants said they felt a lot or much better than before injection.** The researchers noted that no specific safety concerns were reported except expected injection site reactions.

—*Dermatol Surg* 28 (7 Pt 2):1153-61

AUTOLOGOUS FAT, FILLERS EFFECTIVE FOR HIV LIPOATROPHY

Dermal fillers and autologous fat transfer are effective for treatment of HIV associated facial lipodystrophy, with high rates of

RESEARCH BRIEFS



“FDA is very concerned that products distributed by these suppliers may cause harm to patients, because they may be unsafe or ineffective.”

— Thomas J. Christl of the FDA’s Office of Drug Security, Integrity, and Recalls and Office of Compliance, CDER, in a warning letter to physicians who purchased medications from questionable foreign providers. Look for more coverage in the next edition.

Valeant, Galderma Revise Agreement Terms

Valeant Pharmaceuticals International, Inc. reached agreement on terms of a revised North American aesthetics arrangement with Galderma S.A. Under the terms, Galderma will

continue to supply Restylane and Perlane to Valeant, under the terms and conditions that Galderma currently supplies those products to Medicis Pharmaceutical Corporation. In addition, Valeant will make an upfront payment and a royalty to Galderma on sales of Sculptra. Valeant will obtain North American rights to Emervel, a family of hyaluronic acid fillers.

RESEARCH BRIEFS

facial volume restoration and patient satisfaction, a new analysis shows. The analysis included 19 studies involving 724 patients, with 549 patients in the hyaluronic/poly-L-lactic acid cohort, and 175 patients in autologous fat transfer cohort. Although both objective and subjective measures suggested that improvements in facial volume and durability of treatment were similar between dermal fillers and fat transfer, PLLA was reinjected at a rate three-times that of autologous fat. PLLA was also associated with a relatively high rate (22 percent) of subcutaneous papule formation. The authors note that autologous fat transfer offers less of a financial burden as compared to injectable fillers.

— *Plast Reconstr Surg*, 2012, e-pub

LESS PAIN ASSOCIATED WITH ABOBOTULINUMTOXINA WITH PRESERVED SALINE

Reconstitution of abobotulinumtoxinA with preserved saline may result in significantly less pain on injection than with preservative-free saline, according to a new study. In a prospective, randomized, double-blind, side-by-side trial in a private practice dermatology office in Boulder, CO, researchers enlisted 20 volunteer patients to

receive injections on one side of their face with abobotulinumtoxinA reconstituted with preservative-free saline and with abobotulinumtoxinA reconstituted with preserved saline on the other side. Patients reported their pain on a 10-point visual analogue pain scale after each side was injected. Patients kept a diary for the first 48 hours after treatment to track any continued pain, onset of action, or adverse events. Researchers then saw the patients at two-week follow-up visits and recorded any adverse events. They found that **90 percent of patients reported less pain on the side injected with preserved saline than on the side injected with preservative-free saline. In addition, reported pain on the preserved saline side was 60 percent less than on the preservative-free side.** Neither the patients nor the investigators noted any difference in onset of action between the two sides.

— *Dermatol Surg*, 28(6): 867-70

MECHANISMS PROPOSED FOR FACIAL BLANCHING FROM NEUROTOXINS

While facial blanching with neurotoxins therapy has been described in the literature, a new study suggests that skin sites injected with botulinum toxins may not experience the expected



Estimated total value of the North American facial injectables market, comprising botulinum toxin and dermal fillers sold in the US and Canada, by 2017, according to Millennium Research Group's recently released "North American Markets for Facial Injectables 2013" report.

Residency Trends in Cosmetic Dermatology

Sixty seven percent of dermatology resident responding to a recent survey say they have formal lectures focusing on cosmetic dermatology, according to new survey data from the American Academy of Dermatology (AAD; *J Am Acad Dermatol*. e-pub). Lecture topics reported by more than 50 percent of respondents included botulinum toxin injection, lasers, soft tissue augmentation, chemical peels, and sclerotherapy. Topics such as dermabrasion, liposuction, and scar revision were less commonly taught. The most commonly encountered and performed procedures were botulinum toxin injection and lasers (100 percent), followed by soft tissue augmentation (98.8 percent), and encounter both chemical peels and sclerotherapy (95.4 percent). Varying

widely, however, was resident experience performing procedures as the first assistant or as the first surgeon.

Study: Face Product Dyes Pose Health Risks

European researchers are urging formulators to remove two dyes—both possibly used in US products—from skin care products and after-shave, based on a recent study suggesting risk to product users. Brilliant Blue (E133) and Patent Blue (E131), both authorized as cosmetic coloring substances in the EU, have been found to permeate shaved or damaged skin in a recently published study (*Food and Chemical Toxicology*; 52:19-27). The Brilliant Blue dye is FDA approved as an additive for usage in food, drug and cosmetic products. ■

decrease in cutaneous vessel tone associated with higher body temperature. After reviewing normal physiologic responses to heat stress and the role of cholinergic neurotransmission in modulating cutaneous vascular tone, investigators reported a case of a 32-year-old woman who complained of white patches on her forehead at sites of abobotulinumtoxinA injections administered two weeks before presentation. They found that acetylcholine is a primary mediator of cutaneous vasodilatation; certain co-transmitters modulate its effect. Chemical denervation by botulinum toxin appears to interfere with these normal signaling pathways and can provide symptomatic relief to patients with undesirable facial flushing. Conversely, they noted, it may create an unwanted cosmetic effect in patients who desire isolated muscle paresis.

—*Dermatol Surg*. 2012, Dec 17

ONABOTULINUMTOXINA ASSOCIATED WITH SUSTAINED EFFECTS

Treatment of the glabellar lines with onabotulinumtoxinA provides long-lasting results of up to four months, according to a recent study. Researchers analyzed data from four trials with 621 onabotulinumtoxinA-treated (20 U), 84.2 percent were

identified as day-30 responders on the Facial Wrinkle scale (FWS) at maximum contraction. Pooled median duration of effect for day-30 responders was 120 days for FWS at maximum contraction and 131 days for FWS at repose. Higher day 30 SGA scores were correlated with a greater duration of effect on dynamic, but not static lines. **Results indicate that more than 50 percent of respondents demonstrated a sustained clinical effect for four months.** The researchers also found that patient satisfaction increased with duration of effect.

—*Dermatol Surg*; 38(11): 1794-803

COMPARING 1:1.5 DOSE-CONVERSION RATIO FOR INCOBOTULINUMTOXINA AND ONABOTULINUMTOXINA

Increasing the dose of either incobotulinumtoxinA or onabotulinumtoxinA above the 20 U recommended for glabellar frown lines may not yield the desired effect, according to findings from a new study. To investigate the impact of using 50 percent higher dose of onabotulinumtoxinA, researchers enrolled patients with symmetrical moderate to severe glabellar frown lines and treated them with two injects in the corrugator muscles of either 4 u

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—Dr. Matteo Tretti Clementoni
Plastic Surgeon
Milan, Italy

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incobotulinumtoxinA or 6 U onabotulinumtoxinA (equivalent to 20 and 30 U, respectively, if corrugator muscles on both sides and the procerus are treated). They then assessed glabellar frown line severity was from standardized photographs every four weeks for four months and, in a subset of subjects, for up to six months post-treatment. The primary efficacy endpoint was the percentage of subjects with an improvement of greater than one point on the five-point scale at week four. **Response rates showed no added benefit of a 50 percent higher dose of onabotulinumtoxinA at all phases of post-treatment.**

—*J Cosmet Dermatol*; 11(4): 267-71

INCOBOTULINUMTOXIN A FOUND EFFECTIVE FOR AXILLARY AND PALMAR HYPERHIDROSIS

IncobotulinumtoxinA has been found to have positive effects on axillary hyperhidrosis in a recent study, while also conferring benefits when used in combination in combination with a type B botulinum toxin for palmar hyperhidrosis. A total of 84 patients, 58 with axillary and 26 with palmar hyperhidrosis, were included in this open study. Researchers injected axillae with 107 ± 22 U of incobotulinumtoxinA and palms with 213 ± 19 U. They also injected palms with 264 ± 60 U botulinum toxin B over the thenar eminences to avoid muscle weakness. At three-week follow-up post-

treatment, all patients treated for axillary hyperhidrosis reported satisfaction in self-ranking, evaporation decreased by greater than 40 percent, and Dermatology Life Quality Index (DLQI) score improved from 12.0 to 1.7. In the palmar group, 95 percent of patients were satisfied, with more than 50 percent reporting decreased, DLQI score improvement from 10.3 to 1.2. Only one patient in the palmar group experienced muscle weakness, according to investigators.

—*Acta Derm Venereol*. 2012, Oct 11

ABOBOTULINUMTOXINA EFFECTIVE IN SKIN OF COLOR

Tolerability and effectiveness of abobotulinumtoxinA for glabellar lines is similar in patients with skin of color and white patients, according to new findings. Investigators used pooled safety data from six clinical trials from which were derived a safety population (1,869 white patients and 472 patients with skin of color), an efficacy population for a comparison of fixed-dose abobotulinumtoxinA 50 U in white patients and patients with skin of color, and an efficacy population for a comparison of abobotulinumtoxin A adjusted to muscle mass in white and patients with skin of color. Adverse event rates were similar between the two groups, as was onset of effect, however the response rate 30 days after treatment was greater in patients with skin of color than in white patients.

—*Dermatol Surg*. 2012 Nov; 38(11): 1804-11