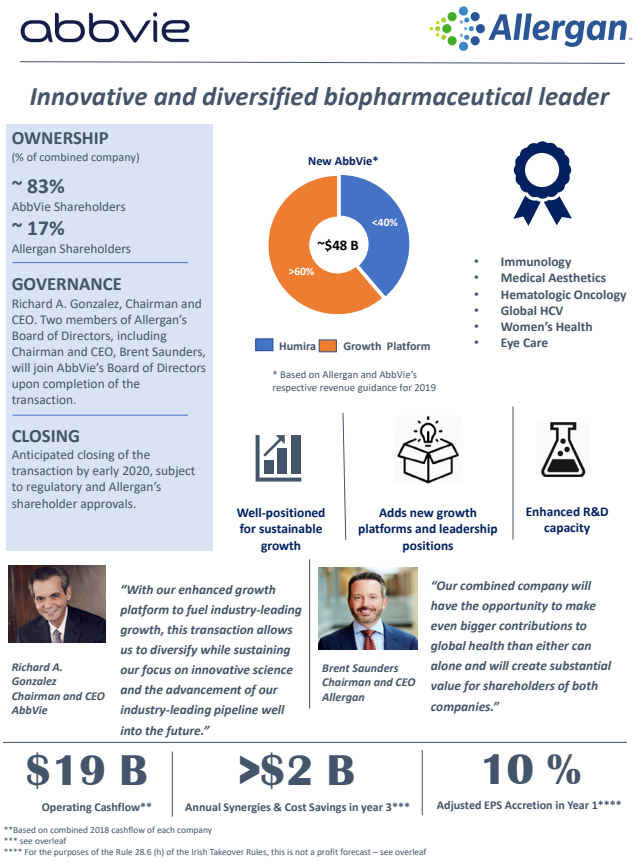
AbbVie to Acquire Allergan

>> AbbVie Inc. and Allergan plc have entered into a definitive transaction agreement under which AbbVie will acquire Allergan in a cash and stock transaction for a transaction equity value of approximately $63 billion, based on the closing price of AbbVie's common stock of $78.45 on June 24, 2019.

"This is a transformational transaction for both companies and achieves unique and complementary strategic objectives," says Richard A. Gonzalez, chairman and chief executive officer, AbbVie. "The combination of AbbVie and Allergan increases our ability to continue to deliver on our mission to patients and shareholders. With our enhanced growth platform to fuel industry-leading growth, this strategy allows us to diversify AbbVie's business while sustaining our focus on innovative science and the advancement of our industry-leading pipeline well into the future."

Under terms of the Transaction Agreement, Allergan Shareholders will receive 0.866 AbbVie Shares and $120.30 in cash for each Allergan Share that they hold, for a total consideration of $188.24 per Allergan Share. The transaction represents a 45 percent premium to the closing price of Allergan's Shares on June 24, 2019.

"This acquisition creates compelling value for Allergan's stakeholders, including our customers, patients and shareholders. With 2019 annual combined revenue of approximately $48 billion, scale in more than 175 countries, an industry-leading R&D pipeline and robust cash flows, our combined company will have the opportunity to make even bigger contributions to global health than either can alone," says Brent Saunders, chairman and chief executive officer, Allergan. "Our fast-growing therapeutic areas, including our world class medical aesthetics, eye care, CNS and gastrointestinal businesses, will enhance AbbVie's strong growth platform and create substantial value for shareholders of both companies."



Upon completion of the transaction, AbbVie will continue to be incorporated in Delaware as AbbVie Inc. and have its principal executive offices in North Chicago, IL, with Richard A. Gonzalez continuing as chairman and chief executive officer. Two members of Allergan's Board, including Brent Saunders, will join AbbVie's Board upon completion of the transaction.

DUOBRII LOTION FOR PLAQUE PSORIASIS HITS SHELVES

Ortho Dermatologics' Duobrii (halobetasol propionate and tazarotene) Lotion, 0.01%/0.045%, is now available. FDA approved in April, Duobrii is the first and only topical lotion that contains a halobetasol propionate and tazarotene in one formulation.

Duobrii Lotion is priced at $825 for a 100-gram tube, which is more than 50 percent less expensive than other branded topical combination products, the company points out. Additionally, through the company's access program, most eligible, commercially insured patients will have a co-pay as little as $25.

"The launch of Duobrii marks the fifth innovative therapy that Ortho Dermatologics has brought forward within the last 30 months," says Bill Humphries, president, Ortho Dermatologics, in a news release. "The Duobrii formulation brings together two well-known ingredients in a unique lotion vehicle with low concentrations of halobetasol propionate and tazarotene, into a single, first-of-its-kind topical treatment. We are proud to provide plaque psoriasis patients this important new option, which offers strong efficacy and an extended duration of use in an

advanced once daily lotion that can be dosed to clearance."

When used separately to treat plaque psoriasis, the duration of use of halobetasol propionate is limited by FDA labeling constraints to two to four weeks duration, and the use of tazarotene can be limited due to tolerability concerns. By combining halobetasol propionate and tazarotene in a patented once-daily moisturizing lotion, however, the Duobrii formulation ensures uniform distribution, allowing for simultaneous contact with the skin surface.

In a year-long safety study, patients used Duobrii for up to 24 weeks of continuous use and up to 52 weeks of as-needed use. Unlike other topical products that either contain steroids or are steroids on their own, Duobrii is not restricted to eight weeks or less of use. The approved labeling for Duobrii does not include a duration limitation; it can be dosed to clearance as long as local skin reactions do not occur, and treatment should be discontinued once clearance is achieved.

"Combination therapy is an important tool in the treatment of plaque psoriasis and, with the launch of Duobrii, I am excited to offer patients a new option that provides the known benefits of a potent topical corticosteroid and a topical retinoid, with synergistic efficacy," says Lawrence J. Green, MD, associate clinical professor of Dermatology, George Washington University School of Medicine, Washington, DC. "Due to its tolerability profile, I believe many psoriasis patients will be able to benefit from the longer duration of use possible with Duobrii."

BIOPHARMX'S BPX-04 PERFORMS WELL IN ROSACEA TRIAL

BioPharmX Corporation 's BPX-04, a novel topical gel formulation of fully solubilized minocycline for the treatment of moderate to severe papulopustular rosacea, performed well in a Phase 2b clinical trial, the company reports.

In the trial, BPX-04, a 1% minocycline gel, successfully met both the primary and secondary endpoints of the trial in demonstrating a statistically significant mean change in the number of facial inflammatory lesions and a two-grade improvement to clear or almost clear on the Investigator's Global Assessment (IGA) scale from baseline to week 12.

"My patients were extremely pleased with their participation in this clinical trial. While the topline results highlight the impressive efficacy of BPX-04, the most compelling takeaway from my experience was my patient's satisfaction with BioPharmX's elegant gel formulation and the lack of irritation that is so commonly experienced with many topical agents. I look forward to the advancement of this promising topical therapy," says Mark Amster, MD, a Brighton MA-based dermatologist and investigator in the clinical trial.

FDA CLEARS ALLERGAN'S COOLTONE DEVICE

The FDA has cleared Allergan plc's CoolTone device for improvement of abdominal tone, strengthening of the abdominal muscles, and development of firmer abdomen. CoolTone is also indicated for strengthening, toning and firming of buttocks and thighs.

Using magnetic muscle stimulation (MMS), CoolTone technology penetrates into the muscle layers and induces involuntary muscle contractions. The body responds to these contractions by strengthening its muscle fibers, resulting in improved muscle conditioning. Whether targeting abdomen, buttocks, or thighs, CoolTone strengthens, tones, and firms the muscles in the treated area, resulting in a more defined and toned appearance. CoolTone has 50 percent more magnetic intensity than the leading competitor (1.35T versus 0.9T) at the point of contact (based on performance testing measuring magnetic field expressed in tesla [T] over the applicator surface.) The clinical significance of this data has not been established.

"By partnering with Allergan, I can offer my patients additional options in body contouring solutions," says Grant Stevens, MD, Founder and Medical Director of Marina Plastic Surgery, Co-Founder and Chief Medical Officer of Orange Twist, and Chairman of the USC-Marina Aesthetic Surgery Fellowship. "CoolSculpting, for non-surgical fat reduction, is one of the most requested treatments in my practice, and now I can introduce my patients to CoolTone for muscle toning, strengthening and firming of the abdomen, buttocks and thighs."

Allergan is now taking orders for the CoolTone device, and first units will ship early in the fourth quarter of this year.

DOMINION AESTHETIC TECHNOLOGIES, INC.'S EON FR SCORES FDA NOD

FDA has cleared Dominion Aesthetic Technologies, Inc.'s eon FR, a non-contact medical device to reduce fat.

The laser energy is delivered using a patent-pending powered articulated arm. The eon FR causes the death of fat cells through apoptosis. The apoptotic process takes six to 12 weeks, and after the eon FR body contouring treatment, the body naturally eliminates fat cells through its lymphatic system. The eon FR treatment takes about 15 minutes to perform with no downtime, the company states.

"I am very pleased that eon FR has received its FDA clearance demonstrating the safety and efficacy of our non-contact, medical device," says Janet Campbell, Founder, Chairman and CEO of Dominion Aesthetic Technologies, Inc, in a news release. "Clearance was secured thanks to our world-class team of laser engineers, scientists, physicist and our incredibly talented scientific advisers who contributed to the study of eon FR."

Ms. Campbell says, "I wish to recognize three physicians who led the clinical study on eon FR: Dr. Thomas Fiala in Orlando, Dr. Jill Waibel in Miami, and Dr. Suzanne Kilmer in Sacramento. All three are members of Dominion's Scientific Advisory Committee."

NEW DATA SUPPORT CLINICAL UTILITY OF DERMTECH'S PLA

A new clinical study confirms the clinical utility of the DermTech's pigmented lesion assay (PLA) in the early detection of melanoma.

The PLA is a non-invasive test that uses molecular gene expression to identify malignant changes in a skin sample collected with adhesive patches. With a demonstrated negative predictive value of 99%, the PLA significantly reduces the probability of missing melanoma to less than 1%, DermTech says.

In a study led by Laura K. Ferris, MD, PhD, of the University of Pittsburgh Medical Center, investigators assessed long-term follow-up after a negative PLA test result. Twelve-month data confirmed the PLA's high negative predictive value.

Data from a patient registry also reported in the study further substantiated the impact of the PLA on clinical decision making. Data collected from 1,575 patients from 62 providers across 40 US dermatology offices in a real-world setting indicated 1,433 PLA negative tests, of which 1,431 (99.9%) were not biopsied during 12 months of follow-up. Of the 142 PLA positive tests identified through the registry, 137 (96.5%) were subsequently biopsied, thus suggesting that physicians use the test results to guide their biopsy decisions.

STUDY: INDOOR TANNING ADDICTION MAY BE LINKED TO GENETIC, PSYCHIATRIC FACTORS

A combination of elevated symptoms of depression along with modifications in a gene responsible for dopamine activity appear to influence an addiction to indoor tanning in young, white non-Hispanic women, a new study suggests. The findings appear in the *Annals of Behavioral Medicine*.

This study compiled survey responses from 292 non-Hispanic white women in the Washington, D.C. area, 18 to 30 years of age, who used indoor tanning beds, sunlamps, or sun booths. The survey asked questions about values and behaviors that might pre-

Remembering Noah Scheinfeld, MD, JD

Hearing the sad news about fellow dermatologist, Noah Scheinfeld, MD, JD, passing away, Practical Dermatology® Chief Medical Editor and Noah Worcester Dermatological Society Secretary/Treasurer Neal Bhatia, MD shared memories in a letter to his fellow Noahites—excerpted here. Read more at PracticalDermatology.com/2019-july.

Many of us knew Noah as a presence, a true individual, and one of the nicest guys around. We all knew him as a dermatologist but he also had a law degree with a sparkling CV and more publications and accolades that we can count. Noah was a real doctor, he took care of patients who needed real help, took on serious medical dermatology diseases, and in many ways made it look easy. He was benevolent as a teacher, masterful as a speaker, and prolific as a writer, just to scratch the surface. His legacy in dermatology will be connected to his work in Hidradenitis Suppurativa, but he was one of the earliest pioneers in the cyber age of dermatology as well. The next time you prescribe any biologic agents for HS, you can thank Noah for opening that door for us because he helped patients this way before we even knew it would be an option. ...

When I heard the news of his death, I sat in my office for a few minutes numb...not just because he meant a lot to the society and to dermatology, not just because he was only three years older than me, and not because it was sudden and we may never know the true cause of his passing...but because we lost our friend, and we won't get to see him again...which is really sad.

We offer our condolences to all of Dr. Scheinfeld's family and friends. Contributions in Dr. Scheinfeld's memory may be made to the Hidradenitis Suppurativa Foundation: hs-foundation.org/donate.

Take 5 with Hermann Lübbert, PhD, CEO, Biofrontera

Founded in Germany as a research platform, Biofrontera began developing dermatologic products and eventually established a focus on photodynamic therapy. It entered the US market with the 2016 approval of Ameluz as part of a photodynamic therapy protocol for actinic keratosis (AK) on the face and scalp. Biofrontera this year acquired Cutanea Life Sciences. The company currently has about 100 employees in the US and plans to increase its sales force to 50 people, including five regional managers, by year's end. Biofrontera CEO Hermann Lübbert, PhD spoke with *Practical Dermatology*® about the company and its future.

1. PDT Has Potential

Hermann Lübbert, PhD: We expect significant calls for PDT in the coming years because there's a large number of patients currently being treated for actinic keratosis, particularly in the US—more in fact than other parts of the world relative to the population density. We think that PDT will achieve a higher market share within that disease, because it can be applied in a field-directed way. Our product is approved for mild to moderate AK on the face and scalp, and it has a very high efficiency and a very good cosmetic outcome.

There are other indications that are currently being researched by dermatological investigators that could add to the potential of PDT beyond just AK. We expect significant growth over the next five to 10 years.

2. Cutanea Offers Opportunities

Dr. Lübbert: What's attractive about Cutanea is that it has two FDA-approved dermatology prescription drugs. These products are commercialized in the US and currently sold to dermatologists, so we can use it to leverage the cost of our sales force in the United States. Aktipak is a line extension product; it comes in a more stable form than the previous versions. But perhaps more exciting is a product called Xepi. Cutanea had licensed Xepi from a Spanish company called Ferrer. This is a new topical antibiotic. It's a new chemical entity without any known existing drug resistance—which often becomes an issue with antibiotics. Within the space of antibiotics this is something that's really exciting. It's very rare that new antibiotics are introduced into dermatology, and the fact that there are no resistances provides to Xepi, we think, great potential.

3. Label Expansions Are a Focus

Dr. Lübbert: We may acquire other products, of course, if a good opportunity arises. But really our major focus is currently—and we think that this will continue for several years—to broaden the labelled indications both for PDT and also for Xepi. Both have, we think, very strong potential indications that are currently untouched by these treatment modalities. We see developing these as a great opportunity to go forward with relatively little risk compared to completely new developments. That's where we are going to put our focus and use our available capital.

4. Biofrontera Wants to Build

Dr. Lübbert: The US is our primary target market. We already have about 70 percent of our revenue coming from this market and we expect this to grow, even in the course of the year. We will continue building the US operation. We are also growing in Germany, but not at the same pace that we grow in the US. Looking forward, we plan to build on our experience and our strong research and development base. At the same time, we will continue building upon our successful and powerful sales force to grow revenues at a consistent ramp.

Revenues have doubled year over year from 2016 worldwide and even more than doubled in the United States. We are still loss-making but we forecast a breakeven point for the fourth quarter of this year. Within the year, we will aim to turn Biofrontera into a profitable small pharmaceutical company, and since we are stock-listed, being profitable should also add additional investor interest to the company.

5. Feedback Matters

Dr. Lübbert: I think it's very important as a company, particularly a small company, to rely on the input and feedback of your customers, and our customers are the dermatologists. When we entered the market or even before we entered the market, we reached out to opinion leaders in the United States for discussions that could help us better understand their needs and the needs of their patients. We had a very positive experience with the dermatology community in the United States from the start, and we hope to continue to build these connections.

dispose a person to a tanning addiction, as well as a series of questions to determine if they had symptoms of depression.

The researchers also collected saliva samples to obtain DNA to look for 34 single nucleotide polymorphisms (SNPs) in five different genes. The specific SNPs that researchers looked at were in genes known to be related to pathways that reward addictive behavior.

"By demonstrating that genes in behavioral reward pathways are associated with tanning addiction, we are providing stronger evidence that tanning addiction is a cancer risk behavior in need of intervention," says lead author Darren Mays, PhD, MPH, an associate professor of oncology and member of the Cancer Prevention and Control Program at Georgetown Lombardi, In a news release. "This

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finding adds to a growing body of evidence from animal studies and neuroimaging studies that have been done in humans."

The researchers adjusted their analyses based on indoor tanning frequency, value of appearance, and depressive symptoms. They found a more than two-fold increased odds of indoor tanning addiction in modifications to the rs4436578 SNP and a slightly less than two-fold increased odds of addiction in modifications to the rs4648318 SNP. When looking at whether the SNPs interacted with depressive symptoms to increase the risk of indoor tanning-addiction, they found a more than 10-fold increase if there were modifications to the rs4436578 SNP and a more than 13-fold increase in the rs4648318 SNP. This knowledge should be helpful if screening for risk of addiction is shown to be beneficial in reducing the chance that people will engage in a cancer-causing activity.

Dr. Mays work in tanning addiction continues with a study, just getting underway, that will explore the effectiveness of text messaging as an intervention to help young women quit if they are addicted to indoor tanning. The research is funded by the Prevent Cancer Foundation.

"This grant will enable us to test behavioral interventions in young women who are addicted to indoor tanning," Dr. Mays says. "We have used text messaging to intervene in other behaviors and have found that the personalized conversation we can deliver through this medium can help people take steps to quit." ■