DREAM DRUGS

These 16 sprouts, from a field of 156, are looking up. With more nurturing, their buds could blossom. **Marc Iskowitz** reports

When the dust settles on another year and analysts take stock, 2014 is set to go down as one of the most interesting in terms of R&D productivity—not just how many drugs the FDA sanctioned, but how valuable they prove commercially.

Thank Gilead's Sovaldi for that. The drug for hepatitis C virus became a blockbuster in record time while raising cure rates, and its recently approved hep. C cousin Harvoni is poised to do well as it sheds ribavirin and interferon from treatment regimens. AbbVie has another interferon- and ribavirin-free regimen waiting in the wings.

The hep. C progress is evidence of one type of industry innovation: "the good old-fashioned wizardry of attacking big problems with big solutions," says Mike Luby, founder, president and CEO of BioPharma Alliance. Others are on the horizon. In the oncology pipeline are PD-1/L1 inhibitors from Bristol-Myers Squibb and AstraZeneca. In neurology, firms are testing BACE inhibitors against Alzheimer's, and in respiratory, investigational drugs from GlaxoSmithKline, Roche and Novartis could lower the steroid burden for patients with severe asthma and COPD.

A second kind of advance has been evolutionary: finding solutions for patients, physicians and payers in what seemed satisfied markets. That's where products and new classes of drugs have led to advances in therapeutic categories, some thought to already be well-served.

Luby points to cardiology as one such category: ACE inhibitors like Vasotec have been mainstays of treating heart failure. New research shows that by switching patients from an ACE inhibitor to Novartis's LCZ696, survival is prolonged.

In the cholesterol area, statins were once reserved for more severe cases. Now, the PCSK9 inhibitors from Amgen and Sanofi/Regeneron may be approved for hard-to-treat patients—and could move into a less and less reserved position. Results of Merck's IMPROVE-IT trial, released last month, "support the notion that the goalposts will move over time, as the science shows greater benefits," says Luby.

It's hard to call psoriasis a satisfied market, although anti-TNFs Enbrel and Humira changed the treatment paradigm, as did IL-12 drug Stelara. Now, Amgen/AstraZeneca, Eli Lilly and Novartis are working on IL-17 drugs that could raise the bar further in psoriasis.

And in diabetes, the GLP-1 and SGLT2 drugs gave doctors new ways to treat this epidemic. Once-weekly versions of some of these same products have altered the patient experience.

In addition to the autoimmune, cardiology, infectious disease, oncology and respiratory sectors, the following pages highlight promising orphan therapies, and outline late-stagers in the metabolic, neurology and women's health areas, and some in other stages. (At press time, Sanofi's Lemtrada received approval for MS, but had yet to launch.)

Profiled agents are based on consultation with *in*Thought, Adis R&D Insight, GfK HealthCare and other experts. Original analysis reflects the latest data sets (as of press time), and is complemented by revenue forecasts, lists of other key products and, where available, the estimated month of launch, plus a percentage giving an indication of the likelihood of success (anything over 50% stands a good chance).

THERAPEUTIC CATEGORIES

Autoimmune

PRODUCTS GENERATING BUZZ

Brodalumab Amgen/AstraZeneca

Indication: Plaque psoriasis/psoriatic arthritis (Ph. III)
What the clinical trials found: In a Phase-III trial vs. Janssen's Stelara (AMAGINE-3), 36% of brodalumab 210mg patients with moderate-to-severe plaque psoriasis vs. 18.5% of the Stelara group achieved PASI 100. No clinically significant safety issues seen.
Credit Suisse Success Probability and *in*Thought Comment: 50%. It looks like Novartis's secukinumab could be the first of the three IL-17 receptors to be approved. What sets brodalumab apart is Amgen's clinical trial program, with head-to-head trials vs. Stelara—that should give reps a talking point. Expected launch: 2016 (Source: Credit Suisse)
Credit Suisse revenue forecast: $371 million in global annual psoriasis sales by 2020
What the physicians are saying: There is limited biologic usage in psoriasis due to the conservative nature of dermatologists and underestimation of severity. Almost a fifth of patients with body surface area of over 10% are classified as mild. However, opportunity for another biologic exists in this market given lack of control with current treatment; about three-fifths of consulting patients are unstable/deteriorating (GfK Disease Atlas 2013 USA). Safety results will trump MOA, although it is recognized that the IL-17 pathway plays a central role in inducing and promoting inflammatory disease processes. *—Alison Rose, therapy lead–immunology, Disease Atlas, GfK*

Lemtrada (alemtuzumab) Sanofi

Indication: Multiple sclerosis (Registered)
What the clinical trials found: After FDA rejected Lemtrada last December, an extension study showed its effects were stable over four years with no new risks. Lemtrada showed effectiveness in relapse reduction and a slowing of physical disability superior to Merck/EMD Serono's Rebif (CARE-MS I, CARE-MS II), and patients were more likely to stay relapse-free for two years. Serious AEs included ITP.
Credit Suisse Success Probability and *in*Thought Comment: 100%. Sanofi has to find patients willing to take the risk. Also, they found the drug works much better early in disease. So it seems patients must decide early on—take Lemtrada, or take other options and completely forego Lemtrada. That's a hard choice for someone in their 30s who was just diagnosed. Expected launch: 2015 (Source: Credit Suisse)
Credit Suisse revenue forecast: $899 million in global annual sales by 2020
What the physicians are saying: Lemtrada is approved in the EU, Canada, Australia and Mexico, and after a delay was approved in the US (at press time). It's still on neurologists' minds: 50% were aware of it on an unaided basis, 85% aided. Neuros most often mention dosing (once- or twice-yearly infusion), very strong efficacy as well as potentially dangerous SEs. Over two-thirds of those aware of the drug see it as an option for later lines of therapy. Neurologists will have patients willing to take the risk, having failed on other treatments, but for Lemtrada to excel, it must be more than a last-resort option. *—Paul Wojciak, research director, health, GfK*

OTHER KEY PRODUCTS IN THE PIPELINE

Daclizumab AbbVie/Biogen Idec
MS (Ph.III)

Adalimumab biosimilar Amgen
RA (Ph.III)

Romosozumab Amgen
Osteoporosis (Ph.III)

Ocrelizumab Biogen Idec/Roche
MS (Ph.III)

Remsima (infliximab biosim) Celltrion
Ankylosing spond./CD/RA (Ph.III)

Etanercept biosimilar Daiichi Sankyo
Plaque psosiasis/RA (Ph.III)

Baracitinib Eli Lilly
RA (Ph.III)

Ixekizumab Eli Lilly
Plaque psoriasis/psoriatic arth. (Ph.III)

Infliximab biosimilar Epirus
RA (Ph.III)

Ertolizumab Genentech
Ulcerative colitis (Ph.III)

Sirukumab Janssen
RA (Ph.III)

Odanacatib Merck
Osteoporosis (Ph.III)

Tildrukizumab Merck
Plaque psoriasis (Ph.III)

Secukinumab Novartis
Plaque psoriasis (Pre-reg.)

Siponimod Novartis
MS (Ph.III)

Fablyn (lasofoxifene) Pfizer
Osteoporosis (Pre-reg.)

Sarilumab Regeneron
RA (Ph.III)

Viviant Pfizer
Osteoporosis (Pre-reg.)

Laquinimod Teva
MS (Ph.III)

Mongersen (GED-0301) Celgene

Indication: Crohn's disease (Ph. II/III)
What the clinical trials found: Ph. II evidence (showcased at UEGW) showed clinical remission and clinical response greater than placebo, with similar AE profile in steroid-dependent/steroid-resistant patients.
Credit Suisse Success Probability and *in*Thought Comment: 70%. Mongersen won't be approved for three years, but we don't have any oral drugs for ulcerative colitis or Crohn's the way we do for RA and—because of Celgene—for psoriasis (Otezla). That would be welcome for those patients. Expected launch: 2019 (Source: Credit Suisse)
Credit Suisse revenue forecast: $1.1B in global annual sales by 2020
What the physicians are saying: Mongersen is a novel therapy with a unique MOA; first-in-class oral antisense therapy. It is assumed Ph.III head-to-head trial will be vs. AbbVie's Humira. Physicians will still compare Mongersen with available TNFs, plus other Ph.II/III competition (e.g. JAKs). To get uptake of oral vs. s/c or IV, Celgene must promote patient convenience and financial gain due to no product wastage/dose escalation. The market must be conditioned to break TNF cycling. *—Alison Rose, therapy lead–immunology, Disease Atlas, GfK*

Cardiology

PRODUCTS GENERATING BUZZ

Acanetrapib Merck

Indication: Atherosclerosis/hypercholesterolemia/hyperlipoproteinemia (Ph.III)

What the clinical trials found: At 24 weeks, anacetrapib decreased LDL-C by 40% and increased HDL-C by 138% in patients already treated with a statin and at guideline-recommended LDL-C goal (DEFINE). CV events occurred in 2% of patients given anacetrapib vs. 2.6% given placebo.

Credit Suisse Success Probability and Comment: 60%. The clinical trial results give researchers confidence to start larger cardiovascular clinical outcomes trials, which is important because an early CETP inhibitor, torcetrapib, was found to cause an excess of deaths and cardiovascular events. Expected launch: 2017 (Source: Credit Suisse)

Credit Suisse revenue forecast: $2.1 billion in global sales by 2020

What the physicians are saying: The drug will have to demonstrate that it doesn't have off-target toxicities. These have plagued other drugs that, ultimately, never made it to the market. Based off its strong clinical performance, in an area that is notoriously difficult to address—HDL—it will likely be a major blockbuster if it can navigate the path to market. Another hurdle will be in proving that the drug reduces CV events. This has largely been taken true but, as we've seen with Zetia, nothing is certain until there's hard data to prove it. *—Alex Bastian, VP, GfK Market Access (health)*

Evolocumab/AMG-145 Amgen

Indication: Hypercholesterolaemia/hyperlipoproteinaemia (Pre-reg.)

What the clinical trials found: Mean LDL-C reduction of 66%-75% (week 10) and 63%-75% (week 12) from baseline vs. placebo group, and a reduction of 38%-45% and 44% vs. ezetimibe-treated groups (LAPLACE-2), as well as statistically significant reductions in LDL-C vs. placebo in patients with HeFH and HoFH (TESLA and RUTHERFORD-2). It's considered safe and tolerable.

Credit Suisse Success Probability: 65%. Expected launch: 2016 (Source: Credit Suisse)

Credit Suisse revenue forecast: $927 million in global annual sales by 2020

What the analysts are saying: Three major factors will impact success in market: 1) long-term data on the potential to reduce CV events; 2) the right market-access strategy that makes prudent trade-offs in access to patients and price, important in a market dominated by cheap statins; and 3) speed. Sanofi and Regeneron made things interesting over the summer when they paid $67.5 million for an FDA voucher to cut rival PCSK9 inhibitor alirocumab's review time down from 10 months to six. Amgen's lawsuit claims that Sanofi and Regeneron stepped on its IP. The three patents in question apply to antibodies to PCSK9, including Amgen's own evolocumab, and the lawsuit seeks to prevent the manufacture, use and sale of Sanofi and Regeneron's similar alirocumab. *—Alex Bastian, VP, GfK Market Access (health)*

OTHER KEY PRODUCTS IN THE PIPELINE

Azimilide Actavis
Ventricular arrhythmias (Ph.III)

Ivabradine Amgen
CHF (Pre-reg.)

Roxadustat AstraZeneca
Anemia in CKD (Ph.III)

Cangrelor AstraZeneca
CAD (Pre-reg.)

Betrixaban Daiichi Sankyo
Thromboembolism (Ph.III)

Edoxaban Daiichi Sankyo
Embolism (Pre-reg.)

Evacetrapib Eli Lilly
CV disorders (Ph.III)

Ranolazine Gilead
Incomplete revascularization (Ph.III)

Darapladib GSK
Atherosclerosis (Ph.III)

Desmoteplase Lundbeck A/S
Stroke (Ph.III)

Cordaptive Merck
Atherosclerosis (Ph.III)

Pradigastat/LCQ908 Novartis
Hyperlipoproteinemia (Ph.III)

Serelaxin Novartis
AHF (Pre-reg.)

Bococizumab/RN-316 Pfizer
Hypercholesterolemia (Ph.III)

Andexanet alfa Portola
FXa inhibitor antidote (Ph.III)

Fostamatinib Rigel
ITP (Ph.III)

CEP-41750 Teva
CHF (Ph.III)

Perindopril/amlodipine XOMA
Hypertension (Pre-reg.)

LCZ696 (Diovan + AHU377) Novartis

Indication: Heart failure/hypertension (Ph. III)

What the clinical trials found: Patients receiving LCZ696 had a 20% reduction in the risk of cardiovascular mortality, a 21% reduction in hospitalizations due to HF and a 16% reduction in the risk of all-cause mortality vs. the enalapril cohort (PARADIGM-HF). There was marginal increase in nonserious angioedema.

Credit Suisse Success Probability: 75%. Expected launch: 2015 (Source: Credit Suisse)

Credit Suisse revenue forecast: $4.2 billion in global annual sales by 2020

What the physicians are saying: Novartis will be entering a cardiovascular marketplace where price-sensitivity has become an increasingly important issue, a consideration that will undoubtedly play a role in the company's price-setting. A month's supply of enalapril costs roughly $4, whereas analysts predict LCZ696 will be priced between $7 and $8 per day (in the US). The drug, however, has demonstrated a compelling clinical profile. It met all of its major endpoints in all the subgroups without raising any sort of a safety signal. Because of this, both market access and pricing strategy will play a key role in the uptake of LCZ696—a potential blockbuster in the making. The way that guidelines incorporate this into the paradigm is also going to be critical. *—Alex Bastian, VP, GfK Market Access (health)*

Infectious Disease

PRODUCTS GENERATING BUZZ

Daclatasvir Bristol-Myers Squibb

Indication: Hepatitis C (Pre-reg.)

What the clinical trials found: Effective when used in combination, including with BMS's own asunaprevir. However, its efficacy appears to be greatest in studies where it was used with Gilead's Sovaldi, achieving cure rates above 90% including among patients with advanced liver disease, GT-3 and those who had previously failed on a protease inhibitor.

Credit Suisse Success Probability: 80%. Expected launch: 2016 (Source: Credit Suisse)

Credit Suisse revenue forecast: $1.4 billion in global annual sales by 2020

What the analysts are saying: Benefits include shorter treatment duration (12 or 24 weeks) compared to 48 weeks of treatment with INF- and RBV-based regimens, and it's been part of an all-oral, INF-free regimen that achieved 100% cure rates. However, given that daclatasvir appears to work best in combination with Solvaldi, the primary competition may in fact be with Johnson & Johnson's Olysio (simeprevir), as it is also often used in combination with the same Gilead product. The "better" combination may be determined by patient subtypes, side effects/tolerability or convenience. —*Michael D'Aust Garcia, SVP, GfK Health*

Veruprevir (ABT-450)/r + ombitasvir (-267) + dasabuvir (-333) AbbVie

Indication: Hepatitis C (Pre-reg.)

What the clinical trials found: SVR12 rates of 99.5% and 99.0% in GT-1b HCV patients in Ph.III, used with or without RBV, respectively (PEARL-III). SVR12 rates were 97% and 90% among GT-1a HCV patients (PEARL-IV).

Bernstein Research revenue forecast: $2.3 billion in global annual sales by 2020

What the analysts are saying: Physicians are excited, particularly by the AbbVie regimen's extremely low discontinuation rates. Given that GT1 is the most common HCV genotype, physicians acknowledge that there is a high unmet need within these patients for better efficacy, safety and oral therapy. But it faces extremely stiff competition, namely from Gilead, which recently introduced Sovaldi (sofosbuvir) and Harvoni (ledipasvir + sofosbuvir), and continues to test other new compounds and various HCV genotypes. Others who are working on compounds in this space include BMS (see above) and Merck, although its grazoprevir + elbasvir combo recently fell short of efficacy goals. Given that all of the new agents appear to contribute to high cure rates, it appears that the fight will likely be won with the better side effects/tolerability, convenience factors (fewer pills) or even potentially on price (Gilead's current pricing is described as "astronomical"). —*Michael D'Aust Garcia, SVP, GfK Health*

OTHER KEY PRODUCTS IN THE PIPELINE

Atazanavir+cobicistat BMS/Gilead
HIV-1 inf. (Pre-reg.)

Brincidofovir Chimerix
Adenovirus inf. (Ph.III)

Elvitegravir+cobicistat+emtricitabine+tenofovir Gilead
HIV/AIDS (Ph.III)

Sofosbuvir+GS-5816 Gilead
HCV inf. (Ph.III)

Tenofovir alafenamide Gilead
HBV inf. (Ph.III)

GSK 1437173A GSK
Herpes (Ph.III)

Cobicistat+darunavir J&J
HIV/AIDS (Pre-reg.)

Actoxumab/bezlotoxumab/MK-3415A Merck
Clost. diff. inf. (Ph.III)

Letermovir/MK-8228 Merck
CMV prophylaxis (Ph.III)

MK-5172A Merck
Hepatitis C (Ph.III)

VZV vaccine/V212 Merck
Herpes zoster (Ph.III)

V419 Merck
Pediatric hexavalent vax (Ph.III)

V503 Merck
HPV-related cancers (Pre-reg.)

Deltyba Otsuka
Tuberculosis (Ph.III)

PF-05212366 Pfizer
Meningitis B vax (Ph.III)

Clostridium difficile Sanofi
Toxoid vaccine (Ph.III)

PR5i Sanofi
DTP-HebB-Polio-Hib (Pre-reg.)

Quadracel Sanofi
Dip-tet-pertusis-polio (Ph.III)

Zmapp Mapp Biopharmaceutical

Indication: Ebola virus infections (clinical)

What the analysts are saying: There is strong interest in ZMapp globally, particularly in the African countries where the Ebola epidemic has been occurring. As of early November, there were 13,000 cases and almost 5,000 deaths—making it the largest and most deadly since the disease was discovered in the '70s—but the CDC estimates that totals could top 500,000 early in 2015. ZMapp was in animal testing, but the Ebola epidemic has spurred tremendous interest and urgency. Even so, only a few hundred doses may be available by the end of 2014. Current formulation of ZMapp involves a cocktail of three monoclonal antibodies, which requires three manufacturing processes; this makes the production complex and requires many partnerships for the small San Diego-based company behind the product, Mapp Biopharmaceutical. There have been no formal studies of ZMapp conducted in humans. A small number of Ebola patients have been given ZMapp on a compassionate-use basis, but the impact of the product on these patients is unclear. Human trials of ZMapp may also face challenges from patients, healthcare professionals and governments who object ethically/morally to using the standard "placebo-controlled study" design in Ebola patients (given the high mortality rate of the disease). —*Michael D'Aust Garcia, SVP, GfK Health*

Oncology

PRODUCTS GENERATING BUZZ

Opdivo (nivolumab) Bristol-Myers Squibb

Indication: 2L NSCLC (Pre-reg.); 1L NSCLC/head + neck/melanoma/RCC (Ph. III)

What the clinical trials found: Ph.III CHECKMATE 037 trial showed slightly more than 20% increase in response rate in melanoma patients previously treated with BMS's Yervoy. The '063 Ph.II 2L/3L lung trial showed ORR of 15% with one-year survival of 41%. AEs were in line with previous trials.

Credit Suisse Success Probability and *in*Thought Comment: 65%. Opdivo is very similar to Merck's anti-PD1 compound, the recently launched Keytruda (pembrolizumab). There's a lot of talk about which one of them is better; we don't know the answer to that yet. Merck did a great job of getting its drug on the market first and it will benefit from that. But it will be interesting to see how the labels compare, as there's potential for Opdivo to work more broadly. In 2015 we will learn a lot very quickly about just how important these drugs are going to be. Expected launch: 1Q 2015 (Source: Credit Suisse)

Credit Suisse revenue forecast: $11.9B in global annual sales by 2020

What the analysts are saying: Based on this very early stage data, it appears that all the different IO agents (Roche's PD-L1 MPDL3280A, AZ's PD-L1 MEDI4736, Merck's PD-1 Keytruda) have similar activities in these respective indications. For lung, response rates for all the different drugs that have been tested so far is around 20%, and they are all relatively well-tolerated, but have slightly different toxicity profiles. So it will be interesting to see how doctors decide to choose these different agents, especially in their current indications as monotherapy. *—Arnold DuBell , PhD, consultant, Kantar Health*

Palbociclib Pfizer

Indication: ER+ breast cancer (Pre-reg.); NSCLC (Ph. II/III)

What the clinical trials found: Phase II PALOMA-1 showed that patients who were given palbociclib and letrozole experienced a significantly longer PFS period (20.2 mos.) vs. patients who received letrozole alone (10.2 mos.). The combination was generally well-tolerated.

Credit Suisse Success Probability and *in*Thought Comment: 80%. This Breakthrough Therapy and Priority Review cancer drug, which has a PDUFA date of April 13, 2015, could be critical to Pfizer's oncology ambitions. It's ahead of, but could compete with, CDK4/6 inhibitors from Novartis (LEE011) and Lilly (abemaciclib), both in Ph.III. Expected launch: 2015 (Source: Credit Suisse)

Credit Suisse revenue forecast: $3.2B in global annual sales by 2020

What the analysts are saying: This once-daily, small-molecule CDK4/6 inhibitor had phenomenal efficacy in terms of PFS benefit and as a result will be very well-received. The only question that doctors will have is that the Ph.II data did not show significant advantage in OS. I do not think doctors will hold that against palbo', given that this was a Ph.II trial and the PFS benefit was so significant and so clinically relevant. It will be approved by FDA in April. *—Arnold DuBell , PhD, consultant, Kantar Health*

OTHER KEY PRODUCTS IN THE PIPELINE

Veliparib AbbVie
Breast/NSCLC (Ph.III)

ABT-199 AbbVie
AML/CLL (Ph.II)

Trebananib Amgen
Ovarian (Ph.III)

Rilotumumab Amgen
Gastric (Ph.III), NSCLC (Ph. II/III)

T-VEC Amgen
Mal. mel. (Pre-reg.)

AZD9292 AstraZeneca
NSCLC (Ph.III)

MEDI4736 AstraZeneca
NSCLC (Ph.III)

Moxetumomab AstraZeneca
Leukemia (Ph.III)

Olaparib AstraZeneca
Ovarian (Pre-reg.) gastric/breast (Ph.III)

Selumetanib AstraZeneca
NSCLC/thyroid. mel.(Ph.III)

Tremelimumab AstraZeneca
Mesothelioma (Ph.III)

Elotuzumab BMS/AbbVie
Multiple myeloma (Ph.III)

Abemaciclib Eli Lilly
Breast (Ph.III)

Necitumumab Eli Lilly
NSCLC (Ph.III)

Idelalisib Gilead
CLL/NHL (Ph.III)

Momelotinib Gilead
Myelofibrosis (Ph.III)

ARN-509 J&J
Prostate (Ph. III)

Daratumumab J&J
Mult. myeloma (Ph.III)

Yondelis J&J
Breast/sarcoma/ovarian (Ph.III)

LBH589 Novartis
Mult. myeloma (Pre-reg.)

LDE225 Novartis
BCC (Pre-reg.)

BKM120 Novartis
Breast (Ph.III)

PKC412 Novartis
AML (Ph.III)

LEE011 Novartis
Breast (Ph.III)

LGX818 Novartis
Mal. mel. (Ph.III)

TKI258 Novartis
Solid tumors (Ph.III)

S-1 Otsuka
Pancreatic (Ph.III)

Sativex Otsuka
Cancer pain (Ph.III)

Inotuzumab Pfizer
ALL (Ph.III)

Alectinib Roche
NSCLC (Ph. III)

Cobimetinib combo Roche
Met. mel. (Ph.III)

MPDL3280A/ RG7446 Roche
NSCLC (Ph. III)

Custirsen Teva
Prostate (Ph.III)

Lipegfilgrastim Teva
NHL (Ph.III)

Respiratory

PRODUCTS GENERATING BUZZ

Bosatria (mepolizumab) GlaxoSmithKline

Indication: Asthma (Pre-reg.)

What the clinical trials found: Reductions in clinically significant exacerbations of asthma vs. placebo were 47% lower for IV mepolizumab and 53% lower for SC mepolizumab (MENSA, Ph.III). Patients with severe eosinophilic asthma who received mepolizumab 100mg SC once a month achieved greater reductions in maintenance oral corticosteroid dose, during weeks 20-24, compared with patients on placebo, while maintaining asthma control (SIRIUS, Ph.III).

Credit Suisse Success Probability: 70%. Expected launch: 2016 (Source: Credit Suisse)

Credit Suisse revenue forecast: $570 million in annual global sales by 2020

What the analysts are saying: Mepolizumab, an interleukin (IL)-5 biologic, offers an attractive proposition for maintenance treatment for patients with severe eosinophilic asthma, identified by a blood eosinophil count. The first challenge will be ensuring that severe asthma patients obtain this reading, making them candidates for treatment. Mepolizumab will also face some competition from Teva and AstraZeneca, meaning it is a race to clearly carve out a new niche as the choice of IL-5 within the treatment community. *—Alex Bastian, VP, GfK Market Access (Health)*

Ultibro (indacaterol/glycopyrrolate) Novartis

Indication: COPD (Ph.III)

What the clinical trials found: Ultibro met the primary endpoint, demonstrating non-inferiority of the Ultibro Breezhaler vs. tiotropium + formoterol in improving health-related quality of life outcomes, as well as the secondary endpoint, demonstrating superiority vs. tiotropium + formoterol by improving lung function (QUANTIFY, Ph.III). Once-daily glycopyrrolate/indacaterol was associated with a 31% reduction in the rate of moderate-to-severe exacerbations, compared with twice daily salmeterol/fluticasone (LANTERN, Ph.III).

Credit Suisse Success Probability: 60%. Expected launch: 2016 (Source: Credit Suisse)

Credit Suisse revenue forecast: $1.5 billion in annual global sales by 2020

What the analysts are saying: Market access will be important for Ultibro. Clinical trials demonstrating superiority over the standard of care comprise a strong market-access lever in pricing and reimbursement negotiations. However, a variety of cheaper alternatives threaten to make this market more sensitive to price and access. Most payers and pulmonologists across the EU5 are open to prescribing generic versions of Seretide (GSK), Symbicort (AZ) and Spiriva (BI) when they launch. Being the first steroid-free dual brochodilator will be useful for treating physicians. However, the importance of updates to guidelines and the change in clinical practice will be key for Ultibro. *—Alex Bastian, VP, GfK Market Access (Health)*

OTHER KEY PRODUCTS IN THE PIPELINE

Masitinib AB Science
Asthma (Ph.III)

Selexipag Actelion
PAH (Ph.III)

Benralizumab AstraZeneca
Asthma/COPD (Ph.III)

Brodalumab AstraZeneca
Severe asthma (Ph.III)

PT003 GFF AstraZeneca
COPD (Ph.III)

PT001 GP AstraZeneca
COPD (Ph.III)

Olodaterol+tiotropium bromide Boehringer Ingelheim
COPD (Pre-reg.)

Aclidinium bromide+formoterol fumarate Forest
COPD (Ph.III)

Ragweed immunotherapy Greer
Allergic rhinitis (Ph.III)

Fluticasone furoate+umeclidinium+vilanterol GSK
COPD (Ph.III)

Vilanterol GSK
COPD (Ph.III)

Esuberaprost LungRx
PAH (Ph.III)

MK-8237 Merck
Allergy (Ph.III)

Formoterol+glycopyrrolate Nektar
COPD (Ph.III)

Inhaled glycopyrrolate Novartis
Asthma/COPD (Ph.III)

Glycopyrrolate+indacaterol Novartis
COPD (Ph.III)

Reslizumab Teva
Asthma (Ph.III)

Lebrikizumab Roche

Indication: Asthma (Ph.III)

What the clinical trials found: Asthma attacks were reduced by 60% in patients in Ph.IIb with a high level of the biomarker periostin, compared with 5% in patients with a low level of periostin (LUTE, VERSE). A 9.1% increase in FEV1 over placebo was seen at 12 weeks in the pooled periostin-high treatment arms, vs. a 2.6% increase over placebo in the periostin-low arms. No clinically important safety signals reported.

Credit Suisse Success Probability: 50%. Expected launch: 2018 (Source: Credit Suisse)

Credit Suisse revenue forecast: $308 million in annual global sales by 2020

What the analysts are saying: A key driver of uptake—and payer coverage—will be the degree to which lebrikizumab reduces exacerbations or the oral corticosteroid dose that severe asthmatics require. This drug also faces the challenges of being a new personalized medicine option in asthma—and the hurdles that come along with shifting the mindset in the diagnosis and treatment of asthma. Obtaining coverage and ease of ordering the associated test will be critical for lebrikizumab. *—Alex Bastian, VP, GfK Market Access (Health)*

Other

PRODUCTS GENERATING BUZZ

NEUROLOGY
MK-8931 Merck

Indication: Alzheimer's disease (Ph.III)

What the clinical trials found: Treatment with oral MK 8931 in a Ph.-I trial of 32 patients with Alzheimer's significantly and dose-dependently lowered CSF beta amyloid levels. The average reduction, at the highest dosage, was more than 80% from baseline. It was generally well-tolerated.

Credit Suisse Success Probability and *in*Thought Comment: 20%. There's been three major approaches taken to plaque-busting in Alzheimer's: 1) trying to prevent the deposition of plaque, or remove it, from the brain, which the anti-Aβ monoclonal antibodies bapineuzumab and solanezumab (still being developed though they didn't work on the first go-round) tried to do; 2) trying to prevent formation of the ingredients of the plaque; and 3) the BACE1 inhibitors like MK-8931 that are also trying to prevent formation of the amyloid beta. It's going to be years before we find out the answer to these BACE inhibitors. They must be tested in very large, long trials in people who are not very sick to begin with. But coming up with something that could slow or halt the progression of AD is still a primary goal in drug development today. We have talked to many experts about the BACE inhibitor, and they all give it about a 50-50 shot. But if it works, it's going to be huge. Expected launch: 2018 (Source: Credit Suisse)

Credit Suisse revenue forecast: $2.3 billion in global annual sales by 2020

What the physicians are saying: Early thoughts by neurologists indicate tempered enthusiasm for the class. Neurologists are excited about a potentially new method of treating and slowing Alzheimer's disease, feeling that it shows great promise. However, with trials ongoing for MK-8931 and the recent failed attempts of other pipeline agents, neurologists are taking a "wait and see" approach before getting too excited. *—Paul Wojciak, research director, lead, GfK Therapeutic Class Dynamics syndicated product line*

ORPHAN
Sebelipase alfa Synageva BioPharma

Indication: Wolman disease (Pre-reg.)

What the clinical trials found: Sebelipase alfa improved markers of liver injury, dyslipidemia and liver fat content—key indicators related to Wolman disease. The Ph. III ARISE trial met its primary endpoint, with 31% (11/36) of patients reaching normal levels of ALT, the study's primary endpoint and one of the markers of liver injury, vs. 7% on placebo. The relative reduction in LDL and non-LDL cholesterol was 28%, vs. 6% to 7% among those in the placebo group. Most AEs were mild and unrelated to sebelipase alfa.

What the analysts are saying: This recombinant human lysosomal acid lipase is being developed as an enzyme replacement therapy to treat lysosomal acid lipase (LAL) deficiency, also known as Wolman disease. Citigroup indicated three concerns surrounding sebelipase alfa's commercial chances. The analyst noted that the "key" questions include, "1) prevalence estimates of LAL deficiency are variable, 2) identification of patients could be challenging as many of the signs and symptoms of LAL deficiency overlap with other conditions, 3) LAL deficiency patients have a range of disease severity and it's unclear which patients would require treatment." These concerns could "result in a slower than expected launch compared to other orphan drug peers." Also, concerns over the pain profile of the product could impact uptake. *—Susan Garfield, SVP, GfK Health – Market Access*

OTHER KEY PRODUCTS IN THE PIPELINE

METABOLIC

Velcacetide/AMG-416 Amgen
Secondary hyperparathyroidism (Ph.III)

Tofogliflozin Genentech
Type 2 diabetes (Ph.III)

Eperzan (albiglutide) GSK
Type 2 diabetes (Pre-reg.)

Basal insulin peglispro Eli Lilly
T1/2 diabetes (Ph.III)

Insulin glargine biosimilar Eli Lilly
T2 diabetes (Pre-reg.)

Ertugliflozin/MK-8835 Merck
Type 2 diabetes (Ph.III)

Omarigliptin/MK-3102 Merck
Type 2 diabetes (Ph.III)

Insulin glargine biosim/MK-1293 Merck
T1/2 diabetes (Ph.III)

Ryzodeg Novo Nordisk
T1/2 diabetes (Pre-reg.)

Tresiba Novo Nordisk
Type 2 diabetes (Pre-reg.)

Xultophy (IDegLira) Novo Nordisk
Type 2 diabetes (Ph.III)

NN1218 Novo Nordisk
T1/2 diabetes (Ph.III)

Semaglutide Novo Nordisk
Type 2 diabetes (Ph.III)

Ertugliflozin Pfizer
Type 2 diabetes (Ph.III)

LixiLan Sanofi
T2 diabetes (Ph.III)

Lyxumia (lixisenatide) Sanofi
T2 diabetes (Ph.III)

Toujeo (U300) Sanofi
T1/2 diabetes (Pre-reg.)

NEUROLOGY

Duopa AbbVie
Parkinson's dis. (Pre-reg.)

Solanezumab Eli Lilly
Alzheimer's (Ph.III)

Tanezumab Eli Lilly
Pain (Ph.III)

LU AE58054 Lundbeck
Alzheimer's (Ph.III)

Suggamadex Merck
Neuromuscular blockade (Pre-reg.)

Brexpiprazole Otsuka
Schizophrenia/MDD (Pre-reg.)

Bitopertin Roche
Schizophrenia (Ph.III)

Gantenerumab Roche
Alzheimer's (Ph.III)

SHP 465 Shire
ADHD (Pre-reg.)

ORPHAN

Miglustat Actelion
Niemann-Pick dis. (Pre-reg.)

Migalastat Amicus
Fabry's disease (Ph.III)

Lumacaftor/ivacaftor Vertex
CF (Pre-reg.)

N8-GP Novo Nordisk
Hemophilia A (Ph.III)

N9-GP Novo Nordisk
Hemophilia B (Ph.III)

WOMEN'S HEALTH

Elagolix AbbVie
Endometriosis (Ph.III)

MK-8962 Merck
Fertility (Pre-reg.)

Menerba United Biotech
Vasomotor sympt. (Ph.III)