BIG-TIME UPSIDE

A peek at 159 aspiring agents, with profiles on 17 that could shoot to stardom. **Rebecca Mayer Knutsen** has the forecast

The most-promising late-stage pipeline drugs are a varied bunch: cancer therapies employing the immune system, PCSK9 inhibitors targeting cholesterol and biosimilars angling to upset biologics' market share. Some will hit the market with a splash, others will crash and burn due to safety/efficacy issues and the rest could fade into obscurity if competitors win the race to market.

When judging the future of clinical candidates, the only important criterion is whether they will change therapy when approved, notes Bernard Munos, senior fellow at FasterCures. Of a potential drug, Munos asks, "Will patients and physicians clamor for it, as they clamor for [Gilead's hep.-C pill] Sovaldi or some of the new cancer drugs?"

These days, changing the standard of care comes with a hefty price tag: The year 2015 saw more industry pricing controversy than ever before—and with the arrival of biosimilars prices may go haywire.

Nonetheless, oncology boasts the most noteworthy R&D innovation of late. "PD-1/L1 inhibitors are the most remarkable accomplishment in years," says Richard Evans, founder of SSR Health.

Roche is looking to add its PD-L1 inhibitor atezolizumab to the mix, getting a boost with FDA's breakthrough therapy designation for NSCLC. And Eli Lilly's CDK 4/6 inhibitor abemaciclib has shown promise for refractory HR+ advanced or metastatic breast cancer.

THERAPEUTIC CATEGORIES

CETP inhibitors have been making headlines in the cardiology sector, though not in a good way. Following the lead of Roche and Pfizer, Eli Lilly became the latest company to halt development. Whither Merck's anacetrapib?

Among PCSK9 inhibitors, analysts are waiting to see if Pfizer's bococizumab can replicate Lipitor's tardy—but huge—splash in the market.

In two pivotal studies Roche's ocrelizumab showed remarkable improvements over an MS standard of care. The humanized mAb could make a real difference if approved.

And R&D dollars are making their way into the orphan-disease space at a greater clip, including BioMarin's agent to generate the muscle protein missing in patients with Duchenne muscular dystrophy.

Advancements in diabetes drugs also grabbed our attention, including Sanofi's lixisenatide/insulin glargine combination.

Perhaps the biggest lingering R&D question involves late-stage biosimilars like Merck/Samsung Bioepis's MK-1293.

"We're still figuring out . . . what the pricing structure will look like for biosimilars in the US," Evans says.

The candidates profiled in this report are based on consultation with *in*Thought, Adis R&D Insight, GfK HealthCare and others. Each therapeutic area includes the latest in clinical data, revenue forecasts, expected launch dates and success likelihood, where available, of featured products.

AUTOIMMUNE

PRODUCTS GENERATING BUZZ

Baricitinib Eli Lilly/Incyte

Indication: RA (Ph.III)

What the clinical trials found: The daily oral demonstrated superiority compared to placebo after 12 weeks based on ACR20 response (Ph. III RA-BEAM). The agent also proved superior to adalimumab on key secondary objectives of ACR20 response and improvement in DAS28-hsCRP score. A few occasional AEs were reported.

Credit Suisse Success Probability and *in*Thought Comment: 70%. The JAK inhibitor appears to have similar efficacy and safety to Pfizer's Xeljanz. It was supposed to have a once daily vs. Xeljanz's twice daily advantage, but Xeljanz's once daily formulation will likely be approved soon. It'll be interesting to see if Lilly/Incyte can do something with patient access and price to improve upon the poor performance of Xeljanz and expand the JAK inhibitor market. Expected launch: 2016 (Source: Credit Suisse)

Credit Suisse forecast: $1.09 billion in global annual sales by 2020

What the physicians are saying: Baricitinib is the most advanced competitor to first-in-class Xeljanz, which caters to patients who have failed anti-TNFs and/or methotrexate; an area where physicians have been awaiting more options. However, price could be a barrier to baricitinib uptake. With the biologic market's expected growth by 2020, JAK inhibitors have room to develop in a market that seeks effective therapies to improve patient quality of life. —*Anita Agier, head of Disease Atlas, GfK Healthcare*

Ozanimod Celgene

Indication: Relapsing MS/ulcerative colitis (Ph.III)

What the clinical trials found: Ozanimod in RMS reduced MRI brain lesion activity and met key secondary MRI-based endpoints (RADIANCE, Ph.II). Ozanimod in UC met all efficacy endpoints with statistical significance in patients on the 1mg dose after 32 weeks of treatment (TOUCHSTONE, Ph.II). No severe AEs observed to date.

Credit Suisse Success Probability and *in*Thought Comment: 25%. The drug looks similar to Gilenya in efficacy and perhaps better in safety. Surprisingly, Novartis never developed Gilenya in ulcerative colitis or Crohn's disease, so ozanimod has a big advantage and will perhaps become an oral alternative to Humira and Entyvio. Expected launch: 2018 (Source: Credit Suisse)

Credit Suisse revenue forecast: $900 million in annual global sales by 2020

What the physicians are saying: Trial findings show ozanimod's ability to reduce MS relapses and brain lesions. Early opinions indicate a similar safety profile to approved oral agents Tecfidera, Gilenya and Sanofi's Aubagio, providing another oral option for needle-adverse patients. If results from ongoing Phase III studies show superiority to Biogen's Avonex and similar or better safety to the current oral therapies, then neurologists could add a formidable weapon to the MS arsenal. —*Paul Wojciak, research director, GfK*

OTHER KEY PRODUCTS IN THE PIPELINE

Romosozumab Amgen/UCB Osteoporosis (Ph.III)

Avatrombopag Astellas Pharma ITP/thrombocytopenia (Ph.III)

Elobixibat AstraZeneca CIC and IBS-C (Ph.III)

Lesinurad AstraZeneca Gout (Ph. III)

Alicaforsen Atlantic Healthcare Pouchitis/ulcerative colitis (Ph.III)

Rituximab biosimilar Boehringer Ingelheim RA (Ph.III)

Mongersen Celgene/Nogra Pharma Crohn's disease (Ph.III)

Etanercept biosimilar Coherus Biosciences/Daiichi Sankyo/Baxalta Plaque psoriasis/RA (Ph.III)

Ixekizumab Eli Lilly Psoriasis (Pre-reg.)

Etrolizumab Genentech Ulcerative colitis/Crohn's (Ph.III)

Guselkumab Janssen Biotech Psoriasis (Ph.III)

Sirukumab Janssen Biotech RA (Ph.III)

Anifrolumab Medarex/MedImmune Systemic lupus erythematosus (Ph.III)

Odanacatib Merck Osteoporosis (Ph.III)

Tildrakizumab Merck Psoriasis (Ph.III)

Siponimod Novartis MS (Ph.III)

Infliximab biosimilar Pfizer RA (Ph.III)

RHB 104 RedHill Biopharma Crohn's disease (Ph.III)

Sarilumad Regeneron RA (Ph.III)

Etrolizumab Roche Ulcerative colitis (Ph.III)

Adalimumab biosimilar Sandoz Plaque psoriasis (Ph.III)

Plecanatide Synergy Chronic constipation/IBS-c (Ph.III)

Laquinimod Teva MS (Ph.III)

ABP 501 (adalimumab biosimilar) Amgen

Indication: RA (Ph.III)

What the clinical trials found: A Phase III trial in patients with moderate-to-severe RA met its primary endpoint of clinical equivalence between the adalimumab biosimilar and branded adalimumab groups, as measured by ACR20 assessment at week 24. The trial also met its key secondary endpoints, including ACR50, ACR70 and DAS 28-CRP. The safety profile was comparable to adalimumab.

***in*Thought Comment:** There are at least 20 biosimilar adalimumab, etanercept and infliximab agents in global development, but the real question is how this will play out in major markets. We expect the market to support no more than four biosimilar versions of a given drug and believe that deals with payers will dictate winners and losers.

What the physicians are saying: Despite concerns that these complex substitutes aren't a perfect replacement, biosimilars will undoubtedly play a leading role in future RA treatment. Most physicians recognize that biosimilars lower costs and give access to a greater number of patients in need of more effective therapies. But a lack of product information and experience will impair their trust. Physician education is one of numerous hurdles the biosimilar will face upon launch as multiple other assets in late phase look to capture a piece of the Humira pie. —*Anita Agier, head of Disease Atlas, GfK Healthcare*

CARDIOLOGY

PRODUCTS GENERATING BUZZ

Bococizumab (RN316) Pfizer

Indication: CV disorders/hypercholesterolemia/hyperlipidemia (Ph.III)

What the clinical trials found: Patients with hyperlipidaemia who were on concurrent statin therapy saw significantly reduced LDL-C at week 12 compared with placebo in a Phase II study. The greatest reductions were observed in patients treated with dose regimens of 150mg twice monthly (-52.4 mg/dL) or 300mg once monthly (-44.9 mg/dL). AEs were similar across placebo and treatment groups.

Credit Suisse Success Probability: 52%. Expected launch: 2018 (Source: Credit Suisse)

Credit Suisse revenue forecast: $747 M in annual global sales by 2020

What the analysts are saying: Bococizumab will have to fight a battle with established products that have provided real-world experience to physicians. Some believe that bococizumab may be able to achieve "best in class" status within the PCSK9 class through its technological partnership with Halozyme. The company's delivery platform promises to improve the efficacy of individual subcutaneous injections and could reduce the required dose, giving bococizumab an edge over alirocumab and evolocumab, which are also administered subcutaneously. Pfizer, the juggernaut that once ruled the cholesterol management arena with Lipitor, has experience with entering disease areas late. Coupled with a legacy in cardiology, bococizumab shouldn't be counted out. *—Alex Bastian, VP, GfK Health*

Anacetrapib Merck

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

What the clinical trials found: Anacetrapib decreased LDL-C (from 81 to 45 vs. 82 to 77 mg/dl for placebo; $p < 0.001$) and increased HDL-C (from 40 to 101 vs. 40 to 46 mg/dl for placebo; $p < 0.001$) at 24 weeks in patients with CHD or CHD risk-equivalent disease (DEFINE Ph.III) with a good cardio safety profile.

Credit Suisse Success Probability and *in*Thought Comment: 60%. The CETP class already has two (well, actually three) strikes, so this is definitely a high-risk/high-reward program. If it works, it'll be HUGE. If it doesn't work, you'll get kicked out of any pharma exec office for even uttering the letters "CETP" for the next 50 years. Expected launch: 2017 (Source: Credit Suisse)

Credit Suisse revenue forecast: $2.09 billion in annual global sales by 2020

What the analysts are saying: CETP inhibition has failed three late-stage tests with Eli Lilly throwing in the towel this past year on their investigational agent—following earlier exits from Roche and Pfizer. The failures, however, have added urgency to Merck's development program to look closely at their own outcomes studies. This includes a futility analysis at the end of the 2016 that could provide a quick answer: Move on or move out. Any drug that can address the clinical needs for better HDL cholesterol and improved outcomes could be a mega blockbuster. Of course if it fails, it will be seen as another R&D flop to add to the pile of other CETP inhibitors. *—Alex Bastian, VP, GfK Health*

Finerenone Bayer

Indication: Congestive heart failure/diabetic nephropathies (Ph.III)

What the clinical trials found: Finerenone was equivalent to eplerenone in reducing a marker of heart failure (NT-PproBNP) and at the optimal dose of 10mg/20mg, there was a 44% reduction in cardiovascular events and mortality. The agent also exhibited signs of a better side-effect profile in the Phase IIb ARTS-HF.

Credit Suisse Success Probability: 25%. Expected launch: 2020 (Source: Credit Suisse)

Credit Suisse revenue forecast: $117 million in annual global sales by 2020

What the physicians are saying: Many doctors are discouraged from using MRAs, including eplerenone and spironolactone, because of the need for monitoring, and it's estimated that only a third of patients who could benefit from these agents actually receive them. Gerasimos Filippatos, MD, from Athens University Hospital Attikon, Greece, said finerenone has greater selectivity for the mineralocorticoid receptor than spironolactone and greater affinity for the receptor than eplerenone. He noted the agent distributes equally to the heart and the kidney, in contrast to eplerenone, which has been shown to distribute primarily to the kidney. In theory, finerenone should demonstrate potency and safety advantages. *—Alex Bastian, VP, GfK Health*

OTHER KEY PRODUCTS IN THE PIPELINE

Revusiran Alnylam FAC (Ph.III)

Beperminogene perplasmid AnGes MD PAD (Ph.III)

Candesartan cilexetil/nifedipine Bayer HealthCare Essential hypertension (Ph.III)

Ularitide Cardiorentis Acute heart failure (Ph.III)

Nebivolol/valsartan Forest Labs Essential hypertension (Ph.III)

Roxadustat FibroGen/Astellas/AstraZeneca Anemia (Ph.III)

Eleclazine Gilead Arrhythmias, hypertrophic cardiomyopathy (Ph.III)

Losmapimod GlaxoSmithKline Acute coronary syndromes (Ph.III)

Volanesorsen Isis Pharmaceuticals hypertriglyceridemia

Vanoxerine Laguna Pharmaceuticals Atrial fibrillation (Ph.III)

Clopidogrel intravenous Ligand Coronary thrombosis (Ph.III)

Pradigastat Novartis Hyperlipoproteinemia (Ph.III)

Andexanet alfa Portola FXa inhibitor antidote (Ph.III)

Betrixaban Portola Venous thromboembolism (Ph.III)

Fostamatinib Rigel CHF (Ph.III)

METABOLIC

PRODUCTS GENERATING BUZZ

LixiLan (lixisenatide/insulin glargine) Sanofi

Indication: Type 2 diabetes (Ph.III)

What the clinical trials found: In a Phase-III trial vs. Sanofi's Lantus, lixisenatide/insulin glargine combination met the primary endpoint of statistically superior reduction in HbA1c (LixiLan-L). The Phase III LixiLan-O trial found the fixed-ratio, once-daily injection of lixisenatide/insulin glargine combination superior to both Lantus (insulin glargine) and Sanofi's Lyxumia (lixisenatide) alone in reducing HbA1c. The combination was well-tolerated with few reported AEs.

Credit Suisse Success Probability: 50%. Expected launch: 2017 (Source: Credit Suisse)

Credit Suisse revenue forecast: $975 million in annual global sales by 2020

What the physicians are saying: Despite new therapy advancements, insulin patients continue to struggle with control. Our data over the past few years have shown an increase in GLP-1 use in combination with insulin, albeit at low levels. Given Lantus's strong standing in the market and the benefits attributable to GLP-1s, physicians will appreciate the convenience of the lixisenatide and Lantus combination. Notably, the addition of a GLP-1 to basal insulin offers the possibility of postprandial control without the risk of weight gain associated with adding a prandial insulin. And, it simplifies the regimen for patients who are already treating several other conditions in addition to diabetes. *—Mary McBride, VP, GfK Roper Diabetes*

Semaglutide Novo Nordisk

Indication: Type 2 diabetes (Ph.III)

What the clinical trials found: The Phase-III SUSTAIN 3 trial showed that once-weekly injection of 1mg semaglutide provided better glycemic control and greater weight loss than 2mg AstraZeneca's Byetta once-weekly. Semaglutide was generally safe and well tolerated.

Credit Suisse Success Probability and *in*Thought Comment: 60%. The GLP-1 inhibitors are slowly emerging as having the best efficacy of the pre-insulin diabetes medicines, but there are already similar weekly formulations on the market. Perhaps this one will have a smaller needle or less injection site pain, but more interesting are the various combinations of GLP-1s with insulins or SGLT2 inhibitors. Expected launch: 2017 (Source: Credit Suisse)

Credit Suisse revenue forecast: $878 million in annual global sales by 2020

What the physicians are saying: The GLP-1 market is increasingly crowded, with several once-weekly subcutaneous injection options already on the market. While GLP-1s have been available for more than a decade, uptake has been slow. Where semaglutide will set itself apart is with its oral formulation (O62175C), currently out of Phase II trials. This will appeal to physicians looking to move needle-adverse patients onto a GLP-1. Recent results from SUSTAIN-2 are favorable for semaglutide's subcutaneous formulation, and if the oral formulation performs well on efficacy and safety, physician uptake will follow. *—Mary McBride, VP, GfK Roper Diabetes*

MK-1293 (insulin glargine biosimilar) Merck/Samsung Bioepis

Indication: Type 1\2 diabetes (Ph.III)

What the clinical trials found: In a Phase III study vs. Sanofi's Lantus, the mean change in hemoglobin A1c (A1C) from baseline after 24 weeks is non-inferior in Type 1 diabetes participants treated with MK-1293 (insulin glargine biosimilar). No major safety issues seen.

***in*Thought Comment:** Biosimilar insulins will be an easier sell to doctors than biosimilars for rheumatoid arthritis or cancer. We expect this to be taken up fairly efficiently, and more importantly, for biosimilar insulins to become cornerstones of diabetes franchises.

What the physicians are saying: Merck and Samsung Bioepis' MK-1293 is one of several insulin glargine biosimilars looking to take share from Lantus. While physicians appreciate the cost savings and expanded insulin options biosimilars will provide, the speed with which physicians are ready to move patients to MK-1293 remains to be seen. Uptake will require strong supporting data and a comfort level that transitioning to a biosimilar will be in the patient's interest. A wait and see attitude will prevail among those requiring reassurance that the differences between MK-1293 and Lantus are not clinically meaningful. Uptake will also be linked to MK-1293's ability to obtain interchangeability status with Lantus at the pharmacy. *—Mary McBride, VP, GfK Roper Diabetes*

OTHER KEY PRODUCTS IN THE PIPELINE

Etelcalcetide/AMG416 Amgen Secondary hyperparathyroidism (Pre-reg.)

SaxaDapa AstraZeneca Type 2 diabetes (Pre-reg.)

Linagliptin/pioglitazone Boehringer/Eli Lilly Type 2 diabetes (Ph.III)

Insulin peglispro Eli Lilly T 1/2 diabetes (Ph.III)

Sotagliflozin Lexicon Type 1 diabetes (Ph.III)

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

O62175C Novo Nordisk T1\2 diabetes (Ph.III)

Pradigastat Novartis FCS (Ph.III)

NN1218 Novo Nordisk T 1/2 diabetes (Ph.III)

Xultophy (IDegLira) Novo Nordisk Type 2 diabetes (Pre-reg)

Ertugliflozin Pfizer/Merck Type 2 diabetes (Ph.III)

Lyxumia (lixisenatide) Sanofi Type 2 diabetes (Pre-reg.)

Zirconium silicate ZS Pharma Hyperkalemia (Ph.III)

ONCOLOGY

PRODUCTS GENERATING BUZZ

Atezolizumab Roche

Indication: Bladder; breast; renal; NSCLC (Ph.III)
What the clinical trials found: A Phase-II study (POPLAR) met its primary endpoint and showed a statistically significant survival benefit compared to chemotherapy (HR = 0.54; p = 0.014) in people with recurrent NSCLC whose tumors expressed medium and high levels of PD-L1, which corresponded with people living 7.7 months longer than people who received docetaxel chemotherapy. AEs were consistent with previous studies.
Credit Suisse Success Probability: 75%. Expected launch: 2016 (Source: Credit Suisse)
Credit Suisse forecast: $4.45 billion in global sales by 2020
What the physicians are saying: While a latecomer to the immunotherapy party, atezolizumab represents a new modification of current immunotherapies in that it targets PD-L1 (rather than PD-1), which is hypothesized to have less off-target toxicity. Urothelial bladder cancer (UBC), in particular, has not seen significant development in decades so any new treatment modalities would be welcome for patients and physicians. A biomarker driven approach in tumors such as NSCLC is well established and PD-L1 testing might be able to smoothly integrate. —*Alex Bastian, VP, GfK Health*

Abemaciclib Eli Lilly

Indication: NSCLC; breast cancer (Ph.III)
What the clinical trials found: A Phase-I trial of abemaciclib found a 49% disease control rate for the 57 evaluable patients with NSCLC, including 2 partial responses and 26 patients with stable disease. The disease control rate for the KRAS-mutant patients was 55% vs. 38% for the KRAS wild-type patients. Leukopenia and neutropenia were the most common grade 3 AEs reported. No grade 4 AEs occurred.
Credit Suisse Success Probability: 65%. Expected launch: 2018 (Source: Credit Suisse)
Credit Suisse forecast: $550 million in global sales by 2020
What the physicians are saying: Abemaciclib is the only CDK inhibitor that has shown promise as a single agent, leading to Breakthrough Therapy designation (in refractory HR+ advanced or metastatic breast cancer). On a pharmacologic basis, this could be best in class. Pfizer's Ibrance (palbociclib) has helped to introduce the drug class into the treatment paradigm. Most patients will be treated with a CDK inhibitor. Other drugs in the class have a week off due to AEs (neutropenias). With abemaciclib, you wouldn't need to stop treatment. —*Alex Bastian, VP, GfK Health*

ABP-215 (bevacizumab biosimilar) Amgen/Allergan

Indication: Advanced NSCLC (Ph.III)
What the clinical trials found: In a Phase-III study, the primary endpoint, overall response rates (ORR), was within the pre-specified margin for ABP-215 compared to bevacizumab, showing clinical equivalence. The secondary endpoints, risk difference of ORR, duration of response and progression-free survival were consistent with the primary endpoints. Safety and immunogenicity of ABP 215 were comparable to bevacizumab.
What the analysts are saying: Branded Avastin (bevacizumab) had sales of $3.3 billion in 1H15, representing a huge opportunity for a biosimilar copy. This agent will provide an alternative for the cost-conscious US physician and payer community. Easier access to bevacizumab could be a welcome addition but this depends on how payers integrate biosimilars into formularies and pathways. Another unanswered question: whether this agent can get all Avastin indications. —*Alex Bastian, VP, GfK Health*

OTHER KEY PRODUCTS IN THE PIPELINE

Venetoclax AbbVie/Roche Chronic lymphocytic leukemia (Ph.III)
Veliparib AbbVie Breast/NSCLC/ovarian (Ph.III) glioblastoma (Ph.II/III)
Encorafenib Array BioPharma Mal. melanoma (Ph.III)
Gilteritinib Astellas AML (Ph.III)
Durvalumab AstraZeneca Head and neck/NSCLC (Ph.III)
Moxetumomab pasudotox AstraZeneca Hairy cell leukemia (Ph.III)
Selumetinib AstraZeneca NSCLC/thyroid (Ph.III)
Tremelimumab AstraZeneca Mesothelioma (Ph.III)
Talazoparib BioMarin Breast (Ph.III)
Volasertib Boehringer Ingelheim AML (Ph.III)
Rituximab biosimilar Boehringer Ingelheim Follicular lymphoma (Ph.III)
Elotuzumab Bristol-Myers/AbbVie Multiple myeloma (Ph.III/Pre-reg.)
Rociletinib Clovis Oncology NSCLC (Pre-reg.)
Napabucasin Dainippon Sumitomo Colorectal/gastric (Ph.III)
Necitumumab Eli Lilly/Bristol-Myers Squibb NSCLC (Pre-reg.)
Nelipepimut S Galena Biopharma Breast (Ph.III)
Daratumumab Genmab/J&J Multiple myeloma (Ph.III/Pre-reg.)
Momelotinib Gilead Sciences Pancreatic (Ph.III)
Zastumotide GlaxoSmithKline Mal. melanoma (Ph.III)
Duvelisib Infinity/AbbVie CLL/follicular lymphoma (Ph.III)
Apalutamide J&J Prostate (Ph.III)
Niraparib Merck/TESARO Breast/ovarian (Ph.III)
Evofosfamide Merck KGaA/Threshold Pancreatic/soft tissue carcinoma (Ph.III)
Eltrapuldencel-T NeoStem Oncology Mal. melanoma (Ph.III)
Alpelisib Novartis Breast (Ph.III)
Buparlisib Novartis Breast (Ph.III)
Midostaurin Novartis AML (Ph.III)
Ribociclib Novartis Breast (Ph.III)
Custirsen OncoGenex NSCLC/prostate (Ph.III)
Bavituximab Peregrine NSCLC (Ph.III)
Inotuzumab ozogamicin Pfizer/UCB ALL (Ph.III)
Taselisib Roche Breast (Ph.III)
Vosaroxin Sunesis AML (Ph.III)
Ixazomib Takeda Oncology Multiple myeloma (Ph.III/Pre-reg.)/amyloidosis (Ph.III)

RESPIRATORY

PRODUCTS GENERATING BUZZ

Benralizumab Kyowa Hakko Kirin/AstraZeneca

Indication: Asthma/COPD (Ph.III)
What the clinical trials found: Patients taking benralizumab vs. placebo in a Phase IIb study saw a significant reduction in asthma exacerbation rate over a one-year period. The study met secondary endpoints with patients experiencing lung function and asthma control improvements as measured by the ACQ-6. Overall, frequencies of AEs were similar for benralizumab and placebo. Common cold and skin reactions at the injection site occurred more frequently with benralizumab than placebo.
Credit Suisse Success Probability: 60%. Expected launch: 2017 (Source: Credit Suisse)
Credit Suisse revenue forecast: $676 million in annual global sales by 2020
What the analysts are saying: Benralizumab is part of a new era of treatments for severe asthma that will provide benefits we haven't had for uncontrolled patients. With few options other than medium- to high-dose inhaled corticosteroids and LABAs, patients suffer from both the emotional and physical burden of extended symptomatic states and multiple hospital visits due to exacerbations. Additional effective therapies are a high-level unmet need in this market. Primary concerns remain around potential safety concerns and identifying patients who will benefit from treatments. Still, most physicians see the clinical value these new entries offer and are optimistic about future patient outcomes. —*Anita Agier, head of Disease Atlas, GfK Healthcare*

Revefenacin Theravance Biopharma/Mylan

Indication: COPD (Ph.III)
What the clinical trials found: Data from the Phase-IIb study showed a rapid onset of action, with a median time to achieve a clinically relevant improvement in lung function (at least 100mL increase in FEV1) of 30 minutes for doses of 88 mcg and above. TD-4208 (revefenacin) also reduced the need for short-acting inhaled rescue medication in a dose-dependent manner. The agent was generally well tolerated and had AE rates similar to placebo.
Credit Suisse Success Probability: 50%. Expected launch: 2019 (Source: Credit Suisse)
Credit Suisse revenue forecast: $225 million in annual global sales by 2020
What the analysts are saying: Communicated as potentially a best-in-class drug and first nebulized LAMA, revefenacin may be desirable for some patient types or by preference. The delivery method is thought to achieve a faster and more effective relief of symptoms. The overall impact on the patient quality of life could be perceptively considerable. However, revefenacin will face the same obstacles as any asset entering into a highly competitive, dynamic and undifferentiated market: What real value will it offer compared to current therapies, and at what price? —*Anita Agier, head of Disease Atlas, GfK Healthcare*

Selexipag Actelion

Indication: PAH (Pre-reg.)
What the clinical trials found: Trial results (Ph. III, GRIPHON) showed a 40% decrease in the risk of a morbidity or mortality event, compared with placebo (p < 0.0001), in patients with pulmonary artery hypertension (PAH). All patients had a significant increase of 12 meters in six-minute walk distance at week 26 (p = 0.0027), with an improvement of 34 meters in PAH-treatment naive patients (p = 0.0002). Overall tolerability of selexipag was consistent with prostacyclin therapies.
Credit Suisse Success Probability: 85%. Expected launch: 2016 (Source: Credit Suisse)
Credit Suisse revenue forecast: $982 million in annual global sales by 2020
What the analysts are saying: Selexipag is possibly the most promising new treatment for patients with PAH, a rare and debilitating condition. Its formulation, trial results and novel effects targeting the prostacyclin pathway provide optimism for physicians that patients will be treated more proactively, although the relative effects and long-term outcome benefits compared to current prostacyclin formulations remain a question. —*Anita Agier, head of Disease Atlas, GfK Healthcare*

OTHER KEY PRODUCTS IN THE PIPELINE

Masitinib AB Science Asthma (Ph.III)
Budesonide + formoterol AstraZeneca COPD (Ph.III)
Budesonide + formoterol + glycopyrrolate AstraZeneca COPD (Ph.III)
Formoterol + glycopyrrolate AstraZeneca COPD (Ph.III)
Glycopyrrolate inhaled AstraZeneca COPD (Ph.III)
Tralokinumab AstraZeneca Asthma (Ph.III)
Ciprofloxacin inhalation Bayer HealthCare/Novartis Bronchiectasis (Ph.III)
Fluticasone furoate + umeclidinium + vilanterol GlaxoSmithKline COPD (Ph.III)
Vilanterol GlaxoSmithKline COPD (Ph.III)
Esuberaprost Lung Biotechnology PAH (Ph.III)
Dupilumab Regeneron/Sanofi Asthma (Ph.III)
Lebrikizumab Roche Asthma (Ph.III)
Glycopyrrolate Sunovion Respiratory Development/PARI Pharma COPD (Ph.III)
Luticasone propionate inhalation Teva Asthma (Ph.III)
Reslizumab Teva Asthma (Pre-reg.)
Ivacaftor/VX 661 Vertex Cystic Fibrosis (Ph.III)

OTHER

PRODUCTS GENERATING BUZZ

NEUROLOGY

Ocrelizumab Roche

Indication: Multiple sclerosis (Ph.III)

What the clinical trials found: OPERA I and OPERA II studies (Ph. III) met primary endpoint with a nearly 50% reduction in annualized relapse rate over a two-year period. Overall, AEs were similar to interferon beta-1a in both studies; the most common AEs were mild to moderate infusion-related reactions.

Credit Suisse Success Probability and *in*Thought Comment: 60%. After 15 years in development with failures in RA and lupus, this Rituxan follow-on compound appears to be a game changer in MS. In addition to being the first drug that really works in primary progressive MS, it's on track to be a serious threat to all the current relapsing remitting MS drugs. Expected launch: 2017 (Source: Credit Suisse)

Credit Suisse revenue forecast: $2.23 billion in global annual sales by 2020

What the physicians are saying: Based on positive Phase II and Phase III trial results, some neurologists feel that ocrelizumab's efficacy profile could eventually top that of Tysabri (natalizumab). What may separate ocrelizumab from other effective marketed brands is its promising positive data in primary progressive MS, a form of the disease currently with no approved treatments. While trial results also show great promise in the much more prevalent form of MS, relapsing-remitting MS, the product's benefit/risk profile may deter neurologists from calling on the agent too early and reserve it only for more progressive cases of the disease. Even if this is the case, it would be neurologists' first approved therapy for these patients. *—Paul Wojciak, research director, GfK*

ORPHAN

Kyndrisa (drisapersen) BioMarin

Indication: Duchenne muscular dystrophy (Pre-reg.)

What the clinical trials found: A Phase III study (DEMAND III) showed a 49m difference in the six-minute walk test (6MWT) between those on continual active treatment (n = 52) and those who had been on placebo for the first 48 weeks followed by active treatment (n = 31). AEs were consistent with previous trials.

Jefferies revenue forecast: $1.06 billion in global sales by 2021

Credit Suisse Success Probability and Jefferies comment: 50%. Despite imperfect data, our due diligence indicates a likely positive outcome (we assume ~75% probability for success). Expected launch: 2016 (Sources: Credit Suisse; Jefferies)

What the physicians are saying: There are few treatment options for patients and families affected by Duchenne muscular dystrophy (DMD). The FDA has granted BioMarin's drisapersen priority review status and approval is expected in 2016. [Its PDUFA date is scheduled for 12/27/15. —Ed.] Drisapersen targets exon 51 by "skipping" this genetic code and thereby allowing the creation of partially functional dystrophin, the muscle protein missing in DMD. It is estimated that 13% of DMD's population will benefit from this treatment. It's not a cure, but physicians are expected to welcome this drug into their limited armamentarium as well as Sarepta Therapeutic's eteplirsen, which has a similar mechanism of action. *—Joanne French, VP, new products, GfK*

OTHER KEY PRODUCTS IN THE PIPELINE

INFECTIOUS DISEASE

Asunaprevir+beclabuvir+daclatasvir BMS Hepatitis C (Ph.III)

Fostemsavir BMS HIV-1 inf. (Ph.III)

PRO 140 CytoDyn HIV/AIDS (Ph. III)

Emtricitabine+tenofovir alafenamide Gilead T1/2 diabetes (Ph.III)

Insulin glargine biosimilar Eli Lilly HIV-1 inf. (Ph.III)

Tenofovir alafenamide Gilead Hepatitis B (Ph.III)

GSK 1437173A GlaxoSmithKline Herpes (Ph.III)

Tafenoquine GlaxoSmithKline Malaria (Ph.III)

Dolutegravir+rilpivirine Janssen/ViiV Healthcare HIV/AIDS (Ph.III)

Actoxumab + bezlotoxumab Merck Clost. diff. inf. (Ph.III)

Doravirine+lamivudine+tenofovir disoproxil fumarate Merck HIV-1 inf. (Ph.III)

Elbasvir/grazoprevir Merck Hepatitis C (Pre-reg.)

rVSV S GP/VP40 Merck/NewLink Genetics Ebola (Ph.III)

PR5I Merck/Sanofi DTP-HebB-Polio-Hib (Pre-reg.)

V 212 Merck Herpes zoster (Ph.III)

Amoxicillin+omeprazole+rifabutin RedHill BioPharma Helicobacter inf. (Ph.III)

Eravacycline Tetraphase cUTI/cIAI (Ph.III)

ORPHAN

Firdapse Catalyst LEMS(Pre-reg.), CMS (Ph.III)

AG-221 Celgene AML (Ph.III)

Farletuzumab Eisai/Ludwig Institute for Cancer Research Ovarian cancer (Ph.III)

ISIS TTRRx GSK/ISIS Amyloid polyneuropathy (Ph.III)

AG-221 Infinity CLL (Ph.III)

Obeticholic acid Intercept Primary biliary cirrhosis (Pre-reg.)

NEUROLOGY

Esketamine Acorda Therapeutics Parkinson's (Ph.III)

Buprenorphine/samidorphan Alkermes MDD (Ph.III)

Aducanumab Biogen Alzheimer's (Ph.III)

Brivaracetam UCB Epilepsy (Pre-reg.)

Tanezumab Eli Lilly Pain (Ph.III)

LY 2951742 Eli Lilly Migraine (Ph. III)

Esketamine J&J MDD (Ph.III)

Idalopirdine Lundbeck Alzheimer's (Ph.III)

Gantenerumab Roche Alzheimer's (Ph.III)

Mirogabalin Daiichi Sankyo Fibromyalgia pain (Ph.III)

Oxycodone/naltrexone Pfizer Pain (Pre-reg.)

Pregabalin controlled-release Pfizer Fibromyalgia/postherpetic neuralgia (Ph.III)

WOMEN'S HEALTH

Elagolix AbbVie Endometriosis (Ph.III)

Follitropin alfa biosimilar Allergan/Itero Female infertility (Ph.III)

Bay98-7196 Bayer HealthCare Contraception (Ph.III)

Prasterone vaginal Bayer HealthCare/Endoceutics Vaginal atrophy (Ph.III)

Amphora Evofem Contraception (Pre-reg.)

MK 8342B Merck Contraception (Ph.III)