# Sāls LETTER

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**Novartis' Enbrel beater bounds toward psoriasis approval ahead of the crowd**

Novartis ($NVS) is well on its way to leading a new class of anti-inflammatory treatments, convincing European regulators to recommend approving its injected therapy for psoriasis and putting the company in line for transatlantic launches next year. The European Medicines Agency is putting its weight behind secukinumab, an injected antibody that blocks the an inflammation-related protein called interleukin-17. The recommendation is based on pivotal data in which Novartis' drug significantly reduced the symptoms of psoriasis--and proved superior to Amgen's ($AMGN) blockbuster Enbrel--and full approval usually follows within about three months. The treatment, to be marketed as Cosentyx, is on its way toward a likely FDA approval, as well, winning a unanimous recommendation from an agency panel last month and expecting final word in January. Assuming all goes according to plan, Novartis' injection will be the first IL-17 blocker to hit the market, leading a pack of new treatments that could improve the standard of care for psoriasis, psoriatic arthritis and other inflammatory diseases.

**Novartis cans a researcher whose cooked data led to a slew of retractions**

Novartis ($NVS) has washed its hands of a researcher who admitted to falsifying results in a series of published papers, promising to dig into his work at the company to determine whether the pattern continued in its own labs. As the federal Office of Research Integrity disclosed, former Vanderbilt biomedical researcher Igor Dzhura falsified figures, made up tests and duplicated computer files over a period of years, making studies look much more promising than they were. On the whole, Dzhura admitted to doctoring at least 69 images in 12 figures across 7 publications and three grant applications, according to *Retraction Watch*, forcing him to retract 6 papers printed by *Nature Cell Biology*, *Journal of Physiology* and others. His punishment is a three-year ban from any publicly funded research projects, and, as *Retraction Watch* confirmed, the loss of his position at Novartis' Boston R&D operation. All of Dzhura's admitted frauds took place during his time at Vanderbilt, before he joined Novartis in 2011, but the company has taken swift action to distance itself from him.

**The New War on Cancer:**

**Today's treatments are less invasive with fewer side effects.**

It used to be that the cancer doctor's toolbox contained three essential tools a scalpel to cut out the disease, chemo to poison it and radiation to zap it. But today that toolbox is bulging with new and better weapons. "We're living in an era in which we are able to look at cancer in ways we've never been able to look at it before," said Dr. Peter Rosen, research director at the Disney Family Cancer Center at Providence Saint Joseph Medical Center in Burbank. "In some cases, the results have been almost miraculous."

**Less Radiation:** Radiation can be completed faster than ever sometimes before a patient awakens from surgery. Intraoperative radiotherapy, or IORT, can deliver a single high dose of radiation to the site of a

woman's breast tumor while she is still under anesthesia. The results are just as good as with radiotherapy that lasts several weeks, said Dr. Dennis Holmes, medical director of the new Los Angeles Center for Women's Health at California Hospital Medical Center in downtown Los Angeles.

Ideal candidates for IORT are women with tumors no bigger than a nickel, with no lymph node involvement. At Providence Saint Joseph Medical Center in Burbank, women with early-stage breast cancer can complete a course of radiation in just five days, thanks to a treatment known as SAVI. This therapy uses multiple catheters an improvement over single-catheter systems that are difficult to tailor to a woman's individual anatomy. Among the newest therapies are a vaccine called CDX-110 and a biologic agent called Avastin. But one of the most exciting developments for people with this aggressive form of cancer is a portable battery-operated device worn as a tight-fitting helmet on the head. Developed by an Israeli firm, the NovoTTF delivers alternating electric fields to cancer cells by means of insulated electrodes worn on the scalp, under a white cap. The helmet stunts the growth of tumor cells in patients with reoccurring or progressive brain cancers, without nasty side effects, Lai said.

**The Power of Positive Thinking:** Particularly for women with breast cancer, there's a growing awareness among oncologists of the importance of self-image in the recovery process. A rapidly growing field called oncoplastic surgery seeks not only to preserve the appearance of a woman's breasts but to "even improve them sometimes," Holmes said. For women with breasts that are asymmetrical, saggy or too large, a properly trained oncoplastic surgeon can perform cosmetic work in conjunction with cancer removal, Holmes said.

**A Nurturing Environment:** Cancer centers such as those at Providence Saint Joseph and California Hospital Medical Center are no longer sterile and white-walled dens of sadness and despair. At the Disney Family Cancer Center, patients can mellow out with mood lighting and their choice of music and images projected on curved walls. At the Los Angeles Center for Women's Health, a "patient navigator" helps take care of little tasks that can bedevil a woman's life after surgery, like making sure that the fridge is stocked with fresh food and the bedroom closet has plenty of clean clothes that are easy to put on and take off. These innovations demonstrate that cancer centers are increasingly aware of the importance of environment in treating cancer.

**Novartis' psoriasis drug tops J&J's Stelara as it speeds toward approval**

Novartis' ($NVS) new anti-inflammatory treatment cleared up psoriasis better than Johnson & Johnson's ($JNJ) Stelara in a Phase III trial, a second head-to-head victory for the injectable drug as it nears U.S. and European approvals. In a 679-patient study, Novartis' secukinumab met its primary goal of reducing psoriasis symptoms by at least 90% at 16 weeks, the company said, demonstrating superiority to J&J's treatment. The antibody also met its secondary endpoint of improving the signs of psoriasis by at least 75% after four weeks, according to Novartis.

**Oncothyreon is going it alone with Array's former breast cancer contender**

Moving on from the slow demise of its Merck KGaA-partnered cancer vaccine, Seattle's Oncothyreon ($ONTY) has bought out co-developer Array BioPharma ($ARRY), acquiring exclusive rights to the pair's early-stage breast cancer candidate. Under the deal, Oncothyreon will pay Array $20 million up front for ONT-380, promising "a significant portion" of any sublicensing revenue and another $280 million in milestone payments if it gets acquired in the next three years. Array is also in line for a double-digit royalty on future sales of the drug. In exchange, Oncothyreon gets the sole rights to an oral HER2 inhibitor that "demonstrated an acceptable safety profile" in Phase I and has shown tumor-killing

promise in preclinical studies, the company said. ONT-380 is in the midst of two Phase Ib trials in combination with other agents in heavily pretreated breast cancer patients, and, in preliminary results unveiled Friday, the drug showed early signs of efficacy.

**SPOTLIGHT ON... Jazz heads to the FDA with its $1B rare disease drug**

**Jazz Pharmaceuticals Initiates Rolling NDA Submission For Defibrotide For The Treatment Of Severe Hepatic Veno-Occlusive Disease**

Jazz Pharmaceuticals plc (Nasdaq: JAZZ) today announced the initiation of a rolling submission of a New Drug Application (NDA) to the United States (U.S.) Food and Drug Administration (FDA) for defibrotide for the treatment of severe hepatic veno-occlusive disease (VOD) in patients undergoing hematopoietic stem-cell transplantation (HSCT) therapy. Defibrotide has been granted Fast Track Designation to treat severe VOD by the FDA. The Fast Track Designation is designed to facilitate the development and expedite the review of drugs that treat serious, life-threatening conditions and that address unmet medical needs. The Fast Track process allows a company to submit individual sections of its NDA for review by the FDA as they are completed rather than waiting until the entire application is complete before it can be submitted and reviewed. Earlier this year, Jazz Pharmaceuticals acquired the rights to defibrotide in the U.S. and other markets in North America, South America and Central America. Jazz Pharmaceuticals markets defibrotide in Europe under the name Defitelio® (defibrotide). Defitelio is the first and only licensed product in Europe for the treatment of severe hepatic VOD in patients over one month of age undergoing HSCT therapy.

**Eli Lilly and Adocia agree to develop fast-acting insulin**

U.S. drugmaker Eli Lilly and French biotech Adocia said on Friday they agreed a worldwide licensing partnership to develop an ultra-rapid insulin to treat patients with Type 1 and Type 2 diabetes. The fast-acting insulin, called BioChaperone Lispro, is currently in early-stage Phase Ib studies and aims to control glucose levels better during and after meals. Under the deal, Adocia will receive an upfront fee of $50 million, potential future payments of up to $280 million if BioChaperone Lispro reaches certain development and regulatory milestones, and sales milestones of up to $240 million, the companies said in a statement. Lilly will also pay royalties on sales of the drug, if approved, and reimburse Adocia for some of its research and development expenses, for an unspecified amount. Shares in Adocia jumped 40 percent on the news, trading at 37.70 euros by 0819 GMT (3.19 a.m. EST). Drugmakers Novo Nordisk, Sanofi and Eli Lilly & Co are fiercely fighting for share of the global market for diabetes treatments, worth over $40 billion and growing as over-eating and lack of exercise fuel an epidemic of Type 2 diabetes.

**Novo Nordisk's Tresiba Favored by CHMP for Expanded Use**

**Novo Nordisk** (NVO) announced that the Committee for Medicinal Products for Human Use (CHMP) has recommended Tresiba (once daily basal insulin) for expanded use in patients in the age group of 1 year 17 years who are suffering fromdiabetes. According to the International Diabetes Federation, approximately 497,100 children across the world suffer from type I diabetes with a rise observed in the rate of type II diabetesamong children. Novo Nordisk said that, upon approval, Tresiba can be prescribed to patients suffering from both type I and type II diabetes in the given age group. Tresiba (once-daily) is already approved in Europe as a monotherapy and in combination with oral anti-diabetic medicinal products or mealtime insulin in adults suffering from type I and type II diabetes. Additionally, Tresiba received approval in May 2014 in combination with GLP-1 receptor agonists.

**More Choices Available for Diabetes Management**

Do you have diabetes? Do you notice that your blood glucose (sugar) levels rise or fall quickly? Has your doctor prescribed insulin to treat your diabetes? Are you comfortable with using a medical device? If you answered yes to all of those questions, continuous glucose monitors (CGMs) and insulin pumps are tools that you and your health care professional might consider to assist you in achieving stable blood sugar levels.

***Why managing blood sugar levels is important:***

Diabetes is caused by defects in the body's ability to produce or use insulina hormone that controls blood sugar levels and helps convert food into energy. If the pancreas doesn't make enough insulin, or if the insulin that is produced does not function properly, a person's blood sugar level becomes too high. Over time, that can lead to serious health problems, including: heart attack, stroke, kidney disease, nerve damage, loss of toes or feet, digestive problems, blindness, gum problems and loss of teeth.

Low blood sugar can also be dangerous, causing you to feel shaky or pass out.

*Devices that can help you now*

If you have diabetes, there are several types of devices that can help you keep your blood sugar level within safe ranges. Here are three options you and your healthcare provider may want to consider:

- an insulin pump, which is a computerized device that can deliver a steady flow of insulin, even while you sleep. FDA has cleared and approved many different insulin pumps. The pump, which is similar in size to a pager, is worn outside the body and is connected to a tube (catheter) that carries insulin from the pump to another tube (cannula) implanted just under the skin.
- a continuous glucose monitor (CGM), which uses sensors that measure glucose levels every five minutes in the fluid around your cells (interstitial fluid). The sensor readings, which are sent wirelessly to a receiver, show whether blood sugar levels are rising or falling. Blood glucose meters, which use drops of blood placed on test strips, are approved for use to monitor your blood sugar. The FDA has not yet approved CGM values alone to determine insulin dosing.
- There are also CGM-enabled insulin pumps, which can communicate wirelessly with a CGM sensor. The sensor readings are displayed on the insulin pump screen instead of on a separate receiver, which enables the user to carry one less piece of equipment.

There are currently two FDA-approved, CGM-enabled insulin pumps: the Medtronic MiniMed, approved in April 2006, and the Animas Vibe System, which was approved on Nov. 25, 2014. The Animas Vibe System combines the DexCom G4 Platinum CGM with an Animas insulin pump. This approval gives consumers more choices in the types of CGMs that can be integrated wirelessly with an insulin pump.

“These devices are an important technological advance to address some of the challenges people with diabetes face in managing their blood sugar,” says Alberto Gutierrez, Ph.D., director of FDA's Office of In Vitro Diagnostics and Radiological Health. “As they become better integrated with insulin pumps, CGMs can ease the daily burden of people with diabetes who juggle the use of multiple medical devices.”

***The coming innovation: artificial pancreas***

In addition, researchers are making significant progress towards the development of artificial pancreas device systems (APDS). These automated, closed-loop systems combine a continuous glucose monitor, an insulin infusion pump, and a “smart” system that monitors glucose levels in the body and automatically pumps appropriate doses of insulin when needed, with little or no input from the patient. The ideal APDS will be a system of devices that closely mimics the glucose-regulating function of a healthy pancreas. It will not only monitor glucose levels but

also automatically adjust the delivery of insulin to reduce high blood glucose levels (hyperglycemia) and minimize the incidence of low blood glucose (hypoglycemia). Currently many investigational studies involved in the development of APDS are using sensor enabled pumps, including ones that integrate the G4 Platinum System, as a component. The availability of an insulin pump that is already compatible with the G4 Platinum system will make the development and approval of APDS that use this technology easier. The FDA will continue to prioritize the development of an APDS and will continue to keep you and health care professionals informed of developments.

**What is an artificial pancreas device system (APDS)?**

The ideal APDS will be a system of devices that closely mimics the glucose regulating function of a healthy pancreas. Most researchers in this area are currently studying an APDS consisting of two types of devices already familiar to many people with diabetes: a continuous glucose monitoring system (CGM) and an insulin infusion pump. A blood glucose device (such as a glucose meter) is used to calibrate the CGM.

A computer-controlled algorithm connects the CGM and insulin infusion pump to allow continuous communication between the two devices. Sometimes an artificial pancreas device system is referred to as a “closed-loop” system or an “autonomous system for glycemic control.” In the future, an APDS will not only monitor glucose levels in the body but also automatically adjust the delivery of insulin to reduce high blood glucose levels (hyperglycemia) and minimize the incidence of low blood glucose (hypoglycemia) with little or no input from the patient. The FDA is collaborating with government and private researchers to foster innovation by clarifying agency expectations for clinical studies and product approvals, which will accelerate the development of an APDS. On October 11, the FDA released a final guidance document that addresses requirements for clinical studies and premarket approval applications for and artificial pancreas device system, and provides a flexible regulatory approach that will support the rapid, safe and effective development of artificial pancreas device systems.

**HBR Classics: Sales Reps and the New Commercial Organization**

**Structural transformations in the life sciences industry have put the traditional sales role under increasing scrutiny, with the most prominent change being a drastic reduction in field force deployments in the US and Europe. This, argues Hay Group's Ian Wilcox, is where opportunity lies. By rethinking the role of the sales rep and the new skills it demandsand then executing boldly around a new customer-driven master planpharma companies can put themselves in a prime competitive position.**

Among all the changes that the commercial side of the pharmaceutical industry has undergone in the last decade, the most impactful has been the redistribution of customer influence. There's been a shift away from individual physicians and towards payers (as well as medical institutions and patients). The result of this change? The roles of the sales rep and the commercial organization behind it need to changeand not just incrementally.

Today's customers focus on value. This certainly includes the most time-honored sales factortherapeutic efficacy. But today, cost issues have become more prominent and problem aticcomplicated by different customer needs and different socioeconomic factors. And beyond this, customers are looking for value that extends beyond straight measures of efficacy or costextending to ancillary services that may benefit patients, providers, and payers alike. Examples include resources that make sure patients take the right dosage of their medication, or online tools for medical professionals that are effective and user-friendlyor, better yet, innovative. The classic rep activity of "detailing" a specific product's benefits to customers is now almost an artifact of a previous era.

This information is available in other ways and there are other important factors to emphasize in the new value proposition.

A direction without a roadmap

While there's general agreement on the issues pharma companies face, many executives still aren't clear (or decisive) about how to improve their commercial organizations or the role of the sales rep.

That said, there certainly have been discussions and experiments. For instance, organizations have added required competencies like resilience to the existing rep rolenot a bad thought, but not a bold move either.

Other well-intentioned tactics include: **1. "Delinking" sales force compensation** from sales volume. **2. Moving from the usual "regional sales manager"** model to an "account manager" model that expands the individual rep role. **3. Aggressively leveraging technology** for instance, through so-called e-detailing or Skype sessions or by transitioning the focus of the role to more of an "information broker." **4.** Even **establishing a lower-level rep role** that focuses on dropping samples and keeping contact, while reserving significant interaction for a higher-level rep/team with sophisticated medical knowledge and strategic focus. But in many cases, these kinds of changes just aren't far-reaching enough. They may not be staffed for success. Or, they're moving too slowly (see sidebar).

Pursuing the service model

The rep role that previously focused on exerting influence and providing guidance is now becoming a service model. This means the rep acts as a conduit to help physicians and related customers access information and resources. Dr. David Nash, Dean of the Jefferson Medical University School of Population Health, said "The most disruptive action a pharma company can take is to trump the competition with new and more effective tools to educate the patient. It's very simple: the most sensible investment is one which will contribute to making patients better consumers of medicine."

Back up the commercial organization chain, anecdotal evidence suggests that managers are becoming less focused on "pull through" (numbers of prescriptions) and are managing the business relationship with pharmaco-economic data. When doing this, they use analytical tools to help payers/institutions see how a portfolio of products benefits them.

**The commercial organization.** The commercial organization for 2014 and beyond must: **1.** Connect with customers (through all your services) to make sure you know what they value. **2.** Make sure everyone in your company knows what your customers value (and that they all agree on it). **3.** Focus more on your key accounts than geography. **4.** Arm your sales force with a clear, attractive value proposition that can be communicated at all levelsdescribing what you offer, in both your products and related services. 5. Find ways to open sustainable communications channels, so that you can keep up to date with what your customers want. Work closely with other parts of the organizationespecially R&D, R&D partners, and market access teams.

**The people in sales.** A successful new commercial organization will need people with skills that current reps may not possess. These people are no longer just reps in the classic sense. They provide a conduit of sorts for physicians and other healthcare providers to gain access to resources and tools within their companies' networks. So, what qualities should the core people in sales possess? **1.** A strong medical science background, so they can understand and communicate sophisticated and complex information about advanced therapies. **2.** Outstanding relationship building skills, but more on an institutional level than the interpersonal level that has characterized the traditional rep. **3.** The ability to adapt to changing situations and provide different levels of discourse and service depending on the audience. **4.** A strategic orientation that enables them to confront issues and find solutions at a higher level. **5.** A level of technical knowledge and understanding

that will allow them to team with technical professionals to provide solutions (as opposed to handing them off).

A key factor here is to re-assess current reps for their suitability to this new role. Their previous success working under an old model (likely with performance measures that no longer fit the new role) is no guarantee of future success. Not all will have the new skills, behavioral characteristics, or motivation to be able to develop them quickly enough. Getting moving: Some things to think about companies that rethink the commercial organization correctly in the context of a good understanding of relevant market dynamics and then move the fastest to apply this to the revamped rep role will have the competitive edge.

**What you should do.** To help you work out what you should do, there are some basic steps and questions to consider: **1.** Determine the true level of commitment within your organization to this kind of meaningful change. **2.** Think about the changes in your commercial organization from the years before the economic crisis of 2008-2009 through to today. Which changes would you classify as stopgap and which would you classify as forward thinking? **3.** Which of those stopgap measures (perhaps cuts or re-organization or re-distribution of people) have been re-visited and how? **4.** What effect did the more progressive or experimental changes have? **5.** Where changes weren't successful, what were the reasons? Cultural resistance? Lack of clarity? Not enough people or money? Or were they poorly thought through? **6.** For those changes with potential, how could they be adapted? **7.** Consider the pros and cons of each change. Once you've found a scenario that you think would work, ask yourself whether you have enough of the right people to follow through on it and how you might obtain appropriate resources if you come up short.

Also consider the following: **1.** The work proposition for 2014 and beyondwhat might the career track look like for members of the new commercial organization, particularly reps? **2.** Where will you find your talent?and should you look internally beyond your own commercial organization and externally. outside the pharma industry (or even outside of people with sales/marketing experience)? **3.** Performance measureswhat traditional measures make sense and, almost as importantly, what metrics no longer make sense? **4.** Rewardhow will roles calling for a newoften higher-levelset of talents be priced in the marketplace? And what might the total remuneration implications be?

Fundamental, disruptive changes in the industry require nothing less than a true mindset change. The core commercial organization and its sales rep engine are certainly at the center of any new mindset.

But lasting impactespecially in this mission critical area of sales means: **1.** Getting genuine **commitment** from top management to proceed with the plan. **2.** Assembling a team with the **change management competencies** to move forward. **3.** Producing a **comprehensive analysis** of your organization's strategic and tactical issues around its commercial functionand its relation to other parts of the organization. **4.** Creating an internal **consensus** on what needs to be done, and then incorporating this into a "do-able" blueprint for action.

Tinkering with the structure of the commercial organization or the competency profiles for the sales rep role isn't enough. Game-changing events on the life sciences landscape demand game-changing action from the life sciences industry at its critical point of customer contact: the sales representative.

**Don'ts: In Dress and Personal Habits**

**1.**Don't expectorate. Men in good health do not need to expectorate; with them continual expectoration is simply the result of habit. Men with bronchial or lung disease are compelled to expectorate, but no one should discharge matter of the kind in public place expect into vessels provided to receive it. Spitting upon the floor anywhere is inexcusable. One should not even spit upon the sidewalk, but go to the gutter for the purpose. One must not spit into the fire-place nor upon the carpet, and hence the English rule is for

him to spit in his handkerchief but this is not a pleasant alternative. **2.** Don't whistle in the street, in public vehicles, at the public assemblies, or anywhere where it may annoy people. Best: don't whistle at all. **3.** Don't laugh boisterously. Laugh heartily when the occasion calls for it, but the loud guffaw is not necessary to heartiness. **4.** Don't have the habit of smiling or "grinning" at nothing. Smile or laugh when there is occasion to do either, but at other times keep your mouth shut and your manner composed. People who laugh at everything are commonly capable of nothing.

**WISE MEN'S WISDOM**

**1.**Your reputation is more important than your paycheck, and your integrity is worth more than your career." ------- Ryan Freitas, About.me co-founder. **2.** "Every time we launch a feature, people yell at us." ------ Angelo Sotira, deviant ART co-founder **3.** "Be undeniably good. No marketing effort or social media buzzword can be a substitute for that." ------- Anthony Volodkin, Hype Machine founder **4.** "Money is like gasoline during a road trip. You don't want to run out of gas on your trip, but you're not doing a tour of gas stations." ------- Tim O'Reilly, O'Reilly Media founder and CEO **5.** "Don't worry about people stealing your design work. Worry about the day they stop." ------- Jeffrey Zeldman, A List Apart Publisher **6.** "Chase the vision, not the money, the money will end up following you." ------- Tony Hsieh, Zappos CEO **7.** The value of an idea lies in the using of it." ------- Thomas Edison, General Electric Co-founder



**Sāls Letter wishes its readers a Happy New Year. May 2015 make you happy and prosperous**

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