

Sāls LETTER

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Information and tips for pharmaceutical executives

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Tumor DNA can serve as noninvasive biomarker to stage and help treat cancer

A Johns Hopkins team believes that cell-free circulating tumor DNA can serve as a noninvasive biomarker to help determine a number of things about cancer in the body and aid in its treatment. The Johns Hopkins Kimmel Cancer Center scientists and international colleagues made their conclusion after analyzing blood samples from 640 patients with different types of cancers. Specifically, they identified cell-free circulating tumor DNA, or ctDNA, in the blood of more than 75% of patients who had advanced cancers. They found that same biomarker in patients who had smaller, more localized tumors that hadn't yet spread from their original site, but the percentage reached a much smaller majority. This latter finding could end up being the most significant in terms of using ctDNA as a personalized cancer diagnostic and treatment biomarker tool. For patients with localized tumors, the ctDNA detection worked in 55% of all patient samples, the researchers said, doing above average with colorectal cancer and esophageal cancer. But they enjoyed greater success in patients with metastatic cancers: 82% of patients with solid tumors outside of the brain. That included, in part, detection of 75% of patients with advanced ovarian, colorectal, bladder, gastroesophageal, pancreatic, breast, hepatocellular, head and neck cancers and melanomas. The research highlights the potential of using ctDNA as cancer biomarker, but expect many more studies before the potential for early detection becomes reality.

FDA approves Lundbeck, Takeda antidepressant Brintellix

Danish drugmaker [Lundbeck](#) has been hiring more than 200 sales reps in the U.S. in anticipation of the FDA approval of the blockbuster [antidepressant Brintellix](#). Well, now they have something to sell. Late Monday, the agency said it had put its stamp of approval on the drug for treating depression. "Major depressive disorder can be disabling and can keep a person from functioning normally," said Dr. Mitchell Mathis, acting director of the FDA's Division of Psychiatry Products. "Since medications affect everyone differently, it is important to have a variety of treatment options available for patients who suffer from depression."

Forest Labs wins FDA approval for antidepressant Fetzima

Forest Laboratories took another step forward in rebuilding its antidepressant business with the FDA's approval of Fetzima for major depressive disorder (MDD) in adults. Fetzima, discovered by France's Pierre Fabre Laboratories, is a once-daily serotonin and norepinephrine reuptake inhibitor. New York-based Forest has been seeking new remedies for depression amid generic competition to its antidepressant Lexapro, sales of which have been declining.

Anika pops after the FDA finally approves its arthritis jab

After two stinging rejections sent it back to the lab, Anika Therapeutics ([\\$ANIK](#)) has secured the

FDA's blessing for an osteoarthritis pain injection, propelling the biotech's shares up more than 40%. The drug, Monovisc, is a single-shot formulation of bacteria-derived hyaluronic acid designed to ease knee pain in OA sufferers getting little benefit from analgesics like acetaminophen. The FDA had twice spurned the injection, first in 2010 and then again by denying an appeal in 2012, *Reuters* notes. But Anika retooled its application in the ensuing year and submitted once more in 2013, this time convincing regulators to back its product. The approval sent Anika's shares soaring close to \$50 in premarket trading on Wednesday, reflecting investor confidence that the company can make some noise in a market still littered with multi-injection treatments, including its own Orthovisc. And much of the excitement is tied to Anika's stateside partner: Under an agreement signed in 2011, Johnson & Johnson's ([\\$JNJ](#)) huge Synthes orthopedics business will distribute Monovisc, and the biotech is due a \$5 million milestone upon the first sale with more payments lined up.

Northwest Bio shoots for dendritic success where others have failed

Northwest's brain cancer-treating DCVax-L is like its dendritic forebears in that it uses a patients' own immune cells to attack tumors. However, as the company takes pains to point out, its vaccine differs by using a full set of tumor antigens to target its attack, instead of tapping a pre-selected bunch of biomarkers. That, Northwest believes, makes for a more effective treatment and differentiates DCVax-L from ImmunoCellular's ICT-107, which failed a Phase II trial in glioblastoma in December. Now it's up to Northwest to prove it. After a touch-and-go cash situation forced it to pause enrollment in 2010, the company is in the midst of a 312-patient Phase III study with a primary endpoint of progression-free survival, expecting data by mid 2015.

The FDA is quietly testing some drugs for generic equivalency

[Generics](#) make up about 80% of the drugs U.S. consumers use, but there has long been questions about whether some of them work as well as the products they mimic. Now the [FDA](#) is finding out. The agency since last September has been testing some generic products in labs around the country, a program it started without announcement, *Bloomberg* reports. Kathleen Uhl, acting director of the FDA's Office of Generic Drugs, told the news service that the new fees generic drugmakers are paying are helping to fund the \$20 million effort to expand testing. The new effort follows the agency's finding in 2012 that a generic of Wellbutrin XL, a long-release version of the antidepressant, that was made by Teva Pharmaceutical Industries did not act like the original. Teva pulled its copies, although testing of other Wellbutrin XL copies found them to be equivalent.

Endo's off-label Lidoderm mantra, whistleblower says: 'Put the patch where the pain is'

Ryan filed a [whistleblower](#) suit accusing Endo Health Solutions ([\\$ENDP](#)) sales managers of pushing [Lidoderm](#), a treatment for postherpetic neuralgia (PHN)--a [shingles](#) complication--for other pain problems. Nine years later, it paid off: Last Friday, the company settled three suits with the [Department of Justice](#) for \$193 million, admitting it promoted the pain patch for uses not approved by the [FDA](#) from 2002 to 2006, prosecutors say. The whistleblowers' share of the settlement has yet to be determined; under the False Claims Act (FCA), whistleblowers can receive between 15% and 25% in cases where the government intervenes.

Even for busy doctors, 'nothing is as good as a rep' for getting pharma info

All the surveys and studies tell that doctors like seeing reps, doctors prefer to read, doctors are unduly influenced, doctors aren't, e-detailing will or won't replace reps--probably don't help, either. But you've probably been around long enough to have heard "the sales-rep model is

dead" before. The sales rep isn't dead, just different in some ways--and in others, not different at all. At least that's what former rep and current doctor-scheduling software guy Dan Gilman says. As founder and president of RxVantage, which markets software that allows pharma reps to schedule doctor appointments online, he sees doctors who want the information reps can provide. They and their office staffs just don't want to deal with the logistical hassles.

Lilly's dulaglutide matches Victoza in study, but the real loser is AstraZeneca's Bydureon

Eli Lilly is one step closer to launching its promising new diabetes drug dulaglutide--and one step closer to putting a crimp in Novo Nordisk's big-selling rival, *Victoza*. Lilly unveiled top-line results from a head-to-head trial between its once-weekly Type 2 diabetes remedy and the once-daily *Victoza* (liraglutide). And dulaglutide stood its own. Dulaglutide didn't prove superior to *Victoza*, which would have been ideal for Lilly, if not so much for Novo Nordisk. Few expected that, anyway. But by showing itself equal to the task, and with a convenient weekly dosing schedule, dulaglutide could carve market share away from *Victoza*, which is one of Novo Nordisk's growth mainstays. The drug most threatened by the new data isn't *Victoza*, however. It's *Bydureon*, AstraZeneca's (\$AZN) once-weekly version of exanatide, which went up against *Victoza* in a similar head-to-head trial, and lost.

All three drugs are GLP-1 agonists, and work by stimulating insulin production. Till now, *Victoza* has dominated the category, with about two-thirds share, according to Mark Schoenebaum, an analyst at ISI Group. Schoenebaum estimates the total market for that class at about \$3 billion at present, and \$4 billion to \$5 billion in a few years.

Lilly's dulaglutide hits the mark for comparability to Victoza in a blockbuster showdown

Eli Lilly says its closely watched GLP-1 diabetes drug dulaglutide works as well as the market leading therapy *Victoza*, but isn't superior to the rival drug. That's going to be good enough for Lilly to claim a big win, though, as analysts were ready to hand it a victory on non-inferiority for a once-weekly drug now in the hands of regulators. Lilly handed out the results in advance to a pair of experienced drug reporters at *The Wall Street Journal* and *Reuters*. Sherry Martin, a Lilly senior medical director, told the *Journal's* Peter Loftus that while the results for dulaglutide in AWARD-6 did not demonstrate superiority, measuring changes in HbA1c over 26 weeks, this was the first time another **GLP-1 drug** was shown to be non-inferior to the blockbuster competition.

There wasn't much actual data to pick through early Tuesday. Lilly--which is desperate to win some significant approvals--has a tremendous amount at stake on dulaglutide, perhaps its most important new diabetes drug in a portfolio of new drugs. But in addition to an approval, Lilly also must carve out a significant market share in diabetes, a hotly contested disease with major league competition. And that's where the AWARD-6 head-to-head trial will figure in. Lilly has gone 5 years without any major approval, a dry spell that has coincided with the loss of patent protection on key products.

Peak sales projections for dulaglutide are all over the map. Cowen has pegged the potential at \$700 million, with Bernstein's Tim Anderson projecting \$1.7 billion in 2020. That's not enough to make up for the patent losses, but it would go a long way to providing some credibility for an R&D group that is drawing an increasing level of critical scrutiny. And today's results for Lilly could well boost its projected numbers.

Stand on your two feet!

Sohaib Rabbani Khan

You think everybody does so? Think again. To further confirm this statement, observe the politicians and public speakers who appear on television. A good number of them don't. You will find them shifting their weight from one leg to another. This proves that all of us do not stand on our two feet.

But why so? This is an inside story. The people who do not feel confident enough, those who are nervous and shaky do not stand on their two feet. Have you ever observed gymnastics in Olympic games? They score high on the basis of perfect, firm and unshaken landing or finish on both the feet. That shows confidence. That shows transparency of intention as well. If a person is what he/she is saying he/she will not behave otherwise and will feel solid on the ground. When you are solid on the ground you feel more yourself.

You may call this the inner confrontation or you may even call it hypocrisy, both reducing poise and resilience. You will also find such people more adamant and arrogant. Because they are not well composed of in their personality and behavior. Unsure of themselves, their ideas and thinking. These people always feel inadequate and insufficient no matter how much wealth or fame they have. On the contrary a person having a very transparent personality will behave more confidently and with clear thoughts and ideas.

Sometime there is a tussle in your mind of what you are going to do and what you think should be done. For example you know that bribe is a crime. Whether you take or you pay, its status of illegality does not change. You know that it is wrong in your mind, in your conscious. But for material gain, so that you can prosper in your business or career you do it. Thus you are acting against the social norm and against your own conscious (unless you believe that bribe is not a crime). This is going to make you less confident and shaky.

Stand on your two feet. Keep your conscious clear. Do what you should rather than what is needed for temporary gain despite its unworthiness and questionable or unhealthy status. No gain is more precious than your own peace of mind, than your personal composure and calm. Keep yourself composed and calm, stand on your two feet.

Marketing myths that are killing business

Myth 1: 'Finance should be the centre of solar system'. Truth: The business enterprise has two basic functions – marketing and innovation. Financial magic alone can't do much. *Myth 2:* 'CEOs know a great deal about marketing'. Truth: They know little about marketing and much of what they know is wrong. One good way to spot marketing opportunities is to see what the competitors are doing --- especially if they are doing it successfully. But assuming that they know the way is dangerous. *Myth 3:* 'Management cannot count on public relations to make a measurable contribution to the marketing mix'. Truth: Successful executives know how to demonstrate that they're cost effective. *Myth 4:* You must match price only if you can't offer some other trade off --- features, service, format, delivery etc.

Leaders earn power by caring

Being smart is not enough to be a leader. Subordinates are not impressed by how much a manager knows until after they are convinced that the manager cares enough about their success to lead them to it. But once this bond of caring is formed, subordinates can be motivated to extraordinary efforts based on theirs in the manager's expertise. Example: Ross Perot visited his employees' wives when he was starting his business. He showed them he was aware of the demands he was placing on their families because of the long hours their husbands worked, and asked for their support in making the company successful.

Better communication

To ensure accuracy in communication repeat what the other person says. Repeating the

message succinctly will impress the speaker with your interests in his/her message, and will confirm to both of you that you understand the details of the message.

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Attract new customers

Attract new customers and retain existing ones by constantly providing the company's exceptional expertise. Key: Go beyond recruiting and training great sales reps, encourage them as well as the company's marketing strategists – to constantly inform customers of new industry developments, new ways that products can be used, ways in which the company is improving products etc. Aim: To convince customers that they are doing business with a company that knows its business better than others. That confidence is a powerful builder of customer loyalty.

Shrewder Marketing

Debrief lost customers: A computer service firm sent questionnaires to lost customers asking why they left. It expected few responses, but thought any answer might be useful. Surprise: Over 90% of former customers responded often with detailed information about offers received from the firm's competitors. The firm also discovered that customers had major misconceptions about its products, and how they measured up

o its competitors. Result: The sales force had been retained to better informed customers. Marketing strategy has been changed, sales and profit margins are up.

Turn objections into acceptance: Listen carefully, answer objections completely and in detail . . . Prepare specific countermeasures to overcome problems --- for instance, changes in price, delivery or terms . . . regard yourself as a keeper of your company image --- work to improve mannerism, speech and appearance. Always put a P. S. on sales letters: Research shows conclusively that a postscript gets more attention than any other part of a letter. So, use a postscript of a sentence or two to give the reader an extra reason to agree with your presentation.

Lee Iacocca goes so far as to appoint a contrarian who is instructed to jump into a group policy discussion when opinions seem to be moving one way and take the position of devil's advocate, confronting and testing the validity of the group's line of thinking.

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Winners & Losers

1. A winner paces himself; A loser has only two speeds hysterical and lethargic. **2.** A winner has healthy appreciation of his abilities, and a keen awareness of his limitations; A loser is oblivious both of his true abilities and his true limitations. **3.** A winner takes a big problem and separates it into smaller parts so that it can be easily manipulated; A loser takes a lot of little problems and rolls them together until they are unsolvable. **4.** A winner knows that people will be kind if you give them the chance; A loser feels that people will be unkind if you give them the chance. **5.** A winner tries never to hurt people. and does so only rarely, when it serves a higher purpose; A loser never wants to hurt people intentionally, but does so all the time without even knowing it. **6.** A winner uses amassing only as a means to enjoying; A loser makes amassing an end in itself- therefore, no matter how much the loser amasses, he never looks upon himself as a winner.

Wise Men's Wisdom

As you cherish the things most worthwhile in your family life, cherish the things most worthwhile in your company. --- *W. B. Given*. 'Safety first' has been the motto of the human race for half a million years; but it has never been the motto of leaders. A leader must face danger. He must take the risk and the blame, and the brunt of the storm. --- *Herbert N. Casson*. If a man be endowed with a generous mind, this is the best kind of nobility ---*Plato*. It

is with life as with a play --- it matters not how long the action is spun out, but how good the acting is --- *Seneca*. Those who do the most for the world's advancement are the ones who demand the least --- *Henry L Doherty*. Too many young people itch for what they want without scratching for it --- *Tom D. Taylor*. As the mind must govern the hands, so in every society the man of intelligence must direct the man of labor --- *Johnson*.

Don'ts At Table

1. Don't make a pronounced attempt at correctness of manner; don't be vulgar, but don't on the other hand, show that you are trying hard not to be vulgar. It is better to make mistakes than to be obviously struggling not to make them. **2.** Don't thank host or hostess for your dinner. Express pleasure in the entertainment, when you depart - that is all. **3.** Don't come to breakfast in dishabille. A lady's morning toilet should be simple, but fresh and tasteful, and her hair not in curl-papers. A gentlemen should wear his morning suit, and never his dressing-gown. There are men who sit at table in their shirt-sleeves. This is very vulgar. **4.** Don't, as hostess, follow the English fashion and omit napkins at breakfast. The hardihood with which an Englishman attacks coffee and eggs without a napkin may excite our wonder, but how can the practice be defended? It is anything less than disgusting?

Contents of **Sāls LETTER** are taken from world's best and authentic periodicals e. g. Harvard Business Review (HBR), FDA Consumer. All information are authentic and reliable. We strongly recommend that information and tips mentioned in these pages be adopted and exercised for maximizing management and marketing effectiveness.

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