# THE CANCER LETTER

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*What's in a Suffix?*

## FDA's Dilemma: How to Name Biologics

*By Paul Goldberg*

After a courtroom victory against Amgen Inc. this summer, the last of the obstacles was removed for the first biosimilar agent—a white blood cell growth factor—to enter the U.S. market.

Zarxio (filgrastim-sndz), sponsored by Sandoz Pharmaceuticals, a unit of Novartis, appeared on the U.S. market Sept. 3, offering a lower-priced alternative to the branded product, Neupogen.

With biosimilars about to appear on the market, FDA is preparing to reconsider the manner in which these agents—as well as the reference products they copy—are named.

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## HRSA Publishes Long-Awaited 340B Mega-Rule

*By Matthew Bin Han Ong*

The Health Resources and Services Administration issued the long-awaited "mega-rule" intended to define who qualifies for deep discounts on drug prices under the federal 340B program.

Established in 1992 to benefit hospitals and clinics that serve low-income and uninsured patients, the 340B Drug Pricing Program has expanded exponentially in recent years.

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*In Brief*

## Chad Mirkin Wins Sackler Prize From the National Academy of Sciences

**CHAD MIRKIN** was named the inaugural recipient of the Raymond and Beverly Sackler Prize in Convergence Research by the **National Academy of Sciences**.

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# FDA's Dilemma: How To Name Biologics

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Days before the biosimilar agent became available, on Aug. 28, FDA published a guidance to industry and a related rule that propose changes in the way non-proprietary, or generic, biologics are named. Under the agency's plans, the Sandoz agent would lose the suffix "sndz," an obvious abbreviation for the name of its sponsor, and the Amgen drug would acquire a new suffix.

According to FDA's proposals, the branded filgrastim, which has been on the U.S. market since 1991, would become filgrastim-jcwp and the Sandoz agent would become filgrastim-bflm.

The agency's rationale for assigning suffixes that have no meaning:

"The placement of the identifier as a suffix should result in an originator product, a related biological product, and a biosimilar product being grouped together in electronic databases, yet remaining distinguishable, which should help health care providers identify these products.

"Also, assignment of suffixes to all filgrastim products would help avoid a potential inaccurate perception that filgrastim-sndz, or any other biosimilar product that may be licensed in the future, differs in a clinically meaningful way from its reference product or is inferior for its approved conditions of use."

Asked by this reporter to comment on the agency's new naming policies, Sandoz officials said they welcome "greater clarity from the U.S. Food and Drug Administration on the important topic of nonproprietary naming of biological products." Overall, the sponsors of branded products are happier with the agency's plans for naming (and renaming) of biologics than the makers of biosimilars.

Here, in a nutshell, are proposed a prospective guidance to industry and a related rule that would apply to products now on the market or in the approval pipeline:

• The guidance describes four-letter suffixes to distinguish biosimilars from each other and from reference products. The agency is seeking comment on whether the nonproprietary names of products that have been shown to be interchangeable with the reference products should include a distinct suffix or share the same suffix as the reference product. Zarxio is biosimilar as opposed to interchangeable. Should another sponsor introduce a drug that would meet the higher bar of interchangeability with Amgen's Neupogen, both that agent and the branded drug could end up having the proprietary name filgrastim-jcwp.

• The rule is intended to designate nonproprietary names that contain a suffix for six previously approved products. Each of the six products is either a reference product for an approved or publicly disclosed biosimilar product application, or a biological product that is either biosimilar to, or related to, one of these reference products.

No regulatory pathway existed in the U.S. for generic versions of biologics until the Biologics Price Competition and Innovation Act of 2009 was passed as part of the Affordable Care Act that President Barack Obama signed into law on March 23, 2010.

The BPCI Act created an abbreviated licensure pathway for biological products like Zarxio.

A biosimilar can be licensed if it is shown to have the same mechanism of action, route of administration, dosage form, and strength as the reference biological product. Licensure is possible only for the indications of the reference biological product.

Under this act, products can be deemed either (1) biosimilar or (2) both biosimilar and interchangeable.

The latter category has an advantage: it allows pharmacists to use products interchangeably, without approval by a physician. The Novartis application was submitted for biosimilarity alone—not biosimilarity and interchangeability.

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**Generic Industry: Just Call it "Filgrastim"**

Innovator companies expressed support for the agency's plan to use suffixes to distinguish reference products from biosimilar versions. This would make it easier for FDA to keep track of safety profiles, they said.

The makers of generics were less pleased. Biosimilar products should have the exact same non-proprietary names as reference products in order to encourage substitution.

"PhRMA has long maintained that patient safety should be the paramount concern when considering the naming of biosimilars," Pharmaceutical Research and Manufacturers of America said in a statement. "Distinguishable non-proprietary names will facilitate the attribution of potential adverse events to the correct biologics, which will in turn enable detection of any safety differences between and among biologics.

"Those names will also help ensure that provider decisions regarding treatment choices for individual patients are respected, and prevent errors in the prescribing, dispensing and administration of biologics."

The Biotechnology Industry Organization was similarly pleased.

"We are encouraged by the FDA's proposal to include a unique suffix in the non-proprietary name for biologic products," BIO said in a statement. "Assigning distinguishable product names for all biological products will help to prevent inappropriate substitution, facilitate post-market surveillance of drug safety, ensure accurate attribution of adverse events to the right product, and support tracing of products in the event of the need to recall."

The Biosimilars Council, a unit of Generic Pharmaceutical Association, said FDA's proposals may "erect barriers to patient access to new, more affordable medicines, and jeopardize their safety."

Bert Liang, chairman of the council, said that "biologics and biosimilars should be required to have the same International Nonproprietary Name with no added 'FDA-designated suffix.'"

"Adverse events and product recalls for small-molecule and biologic drugs already are successfully identified using the national drug code, and lot number and company name, and there is no compelling evidence that biosimilars should be handled differently," Liang said in a statement.

"There is already a precedent for shared names (e.g., erythropoietin, somatropin, interferon), which has not resulted in any known patient safety issues. Shared INNs without suffixes are also safely and effectively utilized in EU, Canada, Australia, and Japan. Adding a random collection of letters to the product's nonproprietary name confers no additional safety benefit, and in fact would require the healthcare professional to be armed at all times with a code-breaking reference.

"Moreover, the legislative intent of the biosimilars approval pathway included in the Patient Protection and Affordable Care Act was to support the development of less expensive but equally effective alternatives to biologic drugs. Yet, today's proposals could create an unnecessary barrier to the benefits of FDA-determined interchangeability. Patients, prescribers and dispensers of these drugs need to be able to easily identify which drugs bear a relation to one another in order to maximize the potential savings from the biosimilar approval pathway."

Several groups representing pharmacists and pharmacy benefits managers had previously cautioned against instituting new tracking mechanisms and instituting tracking requirements that "could result in massive confusion among pharmacists, payers, and PBMs and may inhibit patient access to these lifesaving medicines."

**Lower Wholesale Acquisition Cost**

Though Zarxio is the first biosimilar to get on the market, it is not the first follow-on filgrastim.

The agency had previously approved the Teva Oncology drug Granix. Teva has acquired the drug's original sponsor, Sicor Biotech.

"We also are proposing to designate the official name of 'filgrastim-vkzt' for the biological product licensed under BLA 125294, held by Sicor Biotech, UAB, and to change the proper name designated in the license from 'tbo-filgrastim' to 'filgrastim-vkzt,'" the agency said.

"Tbo-filgrastim, marketed as Granix, is a related biological product. FDA has determined that the current names of filgrastim and tbo-filgrastim are not useful within the meaning of section 508 of the FD&C Act. Although these products are distinguished from each other and from filgrastim-sndz [which may become filgrastim-bflm], FDA believes that the addition of a distinguishing suffix to both names, and the elimination of the prefix from tbo-filgrastim, would avoid confusion regarding these products' relationships to one another and to filgrastim-sndz."

It's likely that the makers of biosimilar biologics will not be able to undercut the prices charged for branded agents as dramatically as the makers of generics undercut the prices of small-molecule drugs. With Zarxio just getting on the market, it's too early to see how actual pricing will line up. The picture is further complicated by Granix, which, though not a biosimilar, is another lower-cost alternative.

Here is how the costs and prices line up:

• The Wholesale Acquisition Cost for a 300 mcg syringe of Zarxio is $275.66. The WAC for a 480 mcg syringe is $438.98.

• By way of comparison, the 300 mcg syringe of Neupogen has a WAC of $324.30, and the 480 mcg is priced at $516.40.

• The Average Sales Price for Zarxio doesn't yet exist, but Neupogen's ASP is $288.69 for the 300 mcg injection, and $458.50 for the 480 mcg injection.

• According to the Red Book, the Granix WAC is $246.17 for 300 mcg and $356.74 for 480 mcg. The ASP is $209.58 for the 300 mcg vial, and $335.33 for 480 mcg. According to Teva, Granix GRANIX has gained more than a 34 percent share of the U.S. short-acting G-CSF hospital market in its first 17 months.

Zarxio didn't present significant regulatory dilemma, but being the first biosimilar on the market, it ended up getting bounced to the FDA Oncologic Drugs Advisory Committee on Jan. 7 (The Cancer Letter, Feb. 6).

Zarxio received FDA approval on March 6 (The Cancer Letter, March 6).

To get the agent on the market, Sandoz had to overcome the remaining opposition from Amgen. Finally, on July 21, the United States District Court for the Northern District of California cleared the way for the drug's entry on the U.S. market.

The biosimilar agent has been marketed as Zarzio in Europe since its approval in 2009. According to Sandoz, usage of the drug outside the U.S. adds up to more than 7.5 million days of patient exposure. The Sandoz pivotal head-to-head PIONEER study was the final piece of data contributing to the totality of evidence used by FDA to approve Zarxio as biosimilar to the reference product. Importantly, the data demonstrating high similarity was sufficient to allow extrapolation of use of Zarxio to five indications of the reference product.

"With the launch of Zarxio, we look forward to increasing patient, prescriber and payor access to filgrastim in the U.S. by offering a high-quality, more affordable version of this important oncology medicine," Richard Francis, global head, Sandoz, said in a statement.

The agent is indicated for:

• Patients with cancer receiving myelosuppressive chemotherapy: to decrease the incidence of infection, as manifested by febrile neutropenia, in patients with nonmyeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a significant incidence of severe neutropenia with fever.

• Patients with acute myeloid leukemia receiving induction or consolidation chemotherapy: to reduce the time to neutrophil recovery and the duration of fever, following induction or consolidation chemotherapy treatment of patients with acute myeloid leukemia.

• Patients with cancer undergoing bone marrow transplantation: to reduce the duration of neutropenia and neutropenia-related clinical sequelae, e.g., febrile neutropenia, in patients with nonmyeloid malignancies undergoing myeloablative chemotherapy followed by bone marrow transplantation.

• Patients undergoing autologous peripheral blood progenitor cell collection and therapy: for the mobilization of autologous hematopoietic progenitor cells into the peripheral blood for collection by leukapheresis.

• Patients with severe chronic neutropenia: for chronic administration to reduce the incidence and duration of sequelae of neutropenia (e.g, fever, infections, oropharyngeal ulcers) in symptomatic patients with congenital neutropenia, cyclic neutropenia, or idiopathic neutropenia.

Zarxio's label is posted here.

## HRSA Publishes 340B Megarule Draft, Clarifying Coverage

(Continued from page 1)

Hospitals, clinics and cancer centers rely on it to buy drugs at discounts of as much as 50 percent—and then collect reimbursements that don't reflect the discount. About a third of the country's non-federal hospitals qualify for the program: as of Jan. 1, 2015, there were 11,530 registered and covered entities.

Many key players in oncology have been questioning the program's expansion and its eligibility criteria. According to critics, the program is poorly defined, and is increasingly abused by entities that don't need help from the government.

The 90-page 340B Program Omnibus Guidance published Aug. 28 provides stricter definitions for which patients and entities should be covered—a move that 340B advocates say would limit patient access to drug discounts.

The omnibus is open for public comment through Oct. 27.

"It has been a long time coming," 340B Health, a Washington, D.C. coalition, said in a statement. "There are gray areas in the program and we look forward to having more clarity."

The coalition, formerly called Safety Net

Hospitals for Pharmaceutical Access, a trade group for 340B-enrolled hospitals, represents over 1,000 hospitals.

"This is an important process and it is our hope that safety-net health care providers will not find themselves limited in their ability to meet their mission to treat the underserved," the group said.

The proposed guidance benefits pharmaceutical companies, said 340B Health Communications Vice President Randy Barrett.

"We've gone over it, we continued to dig into some of the details of the analyses and we're talking some of the other organizations in town to see what their analyses are," Barrett said to The Cancer Letter. "A lot of us have come to some fairly different conclusions on it: it's a complicated document.

"As written and as proposed, the guidance would pretty severely limit the hospitals' access to the 340B discounts. And that concerns us greatly, particularly in the area of patient eligibility, where the criteria are much tighter. The other area that's of concern to us is discharge medication—it would apparently outlaw those, and that's definitely a concern.

"So, no, it is not particularly good for hospitals. Everyone is very cautious. Our concern, as we read this thing through now, is that it will limit access to medications for the underserved. The real end loser here is going to be needy folks who we help."

The pharmaceutical industry lobbied heavily for this proposed guidance, Barrett said.

"It certainly benefits pharma in that if you raise the eligibility requirements, it will limit the hospitals' ability to get discounts," Barrett said. "In other words, there will be fewer discounts available, and that certainly leaves pharma with a lot more money. So this is definitely a big plus for them.

"Pharma has put a great deal of effort into the way these proposals have been crafted. There is no question about it. We knew they were working on it, there's no secret. We've been certainly lobbying as well on all these issues and pharma certainly has its right to get their opinion in as well.

"We had heard and understood that this document was going to not be terribly favorable, but what we really see here—if it is enacted as proposed—is a wholesale curtailing of the program."

**PhRMA: Proposed Guidance Would Curb Abuses**

The Pharmaceutical Research and Manufacturers of America, industry's lobby group, applauded the proposed guidance.

"A first look at the guidance indicates both positive signs that HRSA is taking steps to curb abuses of the program as well as some causes for concern," PhRMA said in a statement. "Specifically, PhRMA was pleased to see that the guidance attempts to provide a clearer patient definition, something the Government Accountability Office has recommended and which has the potential to enable better enforcement of program integrity.

"At the same time, the guidance will allow hospitals and other 340B entities that have violated 340B rules to reenter the program with minimal delay, raising questions about whether there are sufficient consequences for entities shown to be violating program rules.

"The guidance also continues to allow hospitals unlimited contract pharmacies despite a Department of Health and Human Services Office of Inspector General report, as well as HRSA's own audits, showing contract pharmacies raise compliance risks and also enrich for-profit pharmacy chains with no clear benefit to patients.

"PhRMA supports the 340B program and hopes future reforms will better enable the program to meet its original goals, which were to improve access to medicines for vulnerable or uninsured patients and not to enrich hospitals and for-profit retail pharmacies."

The American Hospital Association, which represents nearly 5,000 hospitals, health care systems and 43,000 individual members, said it is reviewing the guidance and seeking feedback from 340B member hospitals.

"America's hospitals appreciate HRSA's long-awaited guidance on the vital 340B Drug Pricing Program that provides access to life-saving drugs for those most in need," Ashley Thompson, acting senior executive for policy, said in a statement. "We want to make certain that the new requirements do not over-burden hospitals and strike a balance between hospitals and pharmaceutical companies for ensuring program integrity.

"More importantly, we want to ensure the stability of this program, which has a track record of improving access to care for poor patients and vulnerable communities. We look forward to providing comments to HRSA and working with the agency to strengthen this key program."

**Covered Patients**

According to the current guidance issued in 1996, a "covered patient" must meet the following criteria:

1. The covered entity has established a relationship with the individual, such that it maintains records of the individual's health care;

2. The individual receives health care services from a professional who is either employed by the covered entity or contracted with the hospital or clinic,

such that responsibility for the individual's care remains with the covered entity; and

3. The individual receives care or services from the covered entity that is consistent with the range of services for which the covered entity received federal funding. This requirement does not apply to disproportionate share hospitals.

Critics say 340B covered entities have struggled for years to apply this cryptic definition to the myriad of scenarios under which patients may receive care from a covered entity.

The new mega-rule expands the current three-prong definition to a more specific six-part test:

1. The individual receives a health care service at a facility or clinic site that is registered for the 340B Program and listed in the 340B database.

2. The individual receives a health care service provided by a covered entity provider who is either employed by or is an independent contractor to the covered entity, such that the covered entity may bill for the provider's services.

3. The individual receives a drug that is ordered or prescribed by the covered entity provider described in 2, above. An individual is not considered a patient of the covered entity if their only relationship is the dispensing or infusion of a drug.

4. The individual's health care is consistent with the scope of the Federal grant, project, designation or contract. This requirement does not apply to hospitals.

5. The individual's drug is ordered or prescribed pursuant to a health care service classified as "outpatient." The individual is considered an outpatient (a) if the patient is insured, the care is billed as outpatient to a third party payor, or (b) if the patient is private pay, uninsured or receives charity care, the patient qualifies as an outpatient under the covered entity's policies and procedures.

6. The individual's patient records are accessible to the covered entity and establish that the covered entity is responsible for care.

**Covered Entities**

The proposed guidance clarifies various aspects of covered entity and drug manufacturer compliance, and the update addresses issues of eligibility, registration and termination from the 340B program.

The types of entities eligible for 340B coverage are:

1. Non-hospital entities that receive certain federal grants, federal contracts, federal designations or establish federally funded projects (e.g., FQHCs, family planning clinics, black lung clinics, hemophilia clinics, state-operated AIDS drug purchasing programs and STD clinics);

2. Certain hospital entities that fall into one of the following three categories:

Government owned or operated hospitals;

3. Public or private nonprofit hospitals that have been granted government powers (e.g., authority to tax, issue bonds, provide health care on the government's behalf); or

4. Private non-profit hospitals that contract with state or local government to provide health care services to low-income individuals who are not eligible for Medicare or Medicaid;

5. Children's hospitals;

6. Freestanding cancer hospitals;

7. Rural referral centers; and

8. Sole community hospitals.

**Contract Pharmacies**

In 1996, HRSA extended to entities that did not have an in-house pharmacy to contract with a single outside pharmacy. In April 2010, the agency allowed contracts with multiple pharmacies. According to the agency, over 14,000 pharmacies now dispense 340B drugs.

According to the new proposed guidance: "risk of duplicate discounts can increase with certain drug purchasing and distribution systems, including covered entity contract pharmacy arrangements.

"Therefore, HHS will examine those systems and determine if adjustments have to be made to the system to prevent duplicate discounts. Due to these heightened risks of duplicate discounts, when a contract pharmacy is listed on the public 340B database it will be presumed that the contract pharmacy will not dispense 340B drugs to Medicaid FFS or MCO patients.

"If a covered entity wishes to purchase 340B drugs for its Medicaid FFS or MCO patients and dispense 340B drugs to those patients utilizing a contract pharmacy, the covered entity will provide HHS a written agreement with its contract pharmacy and State Medicaid agency or MCO that describes a system to prevent duplicate discounts.

"Once approved, HHS will list on the public 340B database a contract pharmacy as dispensing 340B drugs for Medicaid FFS and/or MCO patients."

# GAO to Investigate Power Morcellation Harms

*By Matthew Bin Han Ong*

The U.S. Government Accountability Office said it would investigate the controversy stemming from wide use of power morcellators, gynecological devices now known to spread undetected cancers during hysterectomies and myomectomies.

The GAO's Sept. 4 move comes after 12 members of Congress wrote a letter requesting an investigation.

"Hundreds, if not thousands, of women in America are dead because of a medical device known as a laparoscopic power morcellator," the legislators said in the letter Aug. 7. "This device can take a Stage 1 treatable cancer immediately to a Stage 4 terminal cancer. For too many women, this routine procedure ended with a death sentence."

The letter was signed by Reps. Mike Fitzpatrick (R-Pa.), Louise Slaughter (D-N.Y.), Ralph Abraham (R-La.), Rosa DeLauro (D-Conn.), Bill Pascrell, Jr. (D-N.J.), Lou Barletta (R-Pa.), Doug LaMalfa (R-Calif.), Anna G. Eshoo (D-Calif.), Jan Schakowsky (D-Ill.), Chris Smith (R-N.J.), Stephen Lynch (D-Mass.), and Rick Larsen (D-Wash.).

FDA severely limited the use of power morcellators in November 2014, a year after patient advocates Amy Reed and Hooman Noorchashm launched a vigorous campaign that drew FDA's attention to the issue (The Cancer Letter, Nov. 26, 2014).

The GAO investigation comes on the heels of an FBI probe in May. The FBI is reportedly trying to establish whether Johnson & Johnson—one of the largest manufacturers of power morcellators—knew as early as nine years ago that the gynecological device can disseminate uterine cancers (The Cancer Letter, May 29).

It's not publicly known whether a formal FBI investigation has been launched.

The 12 lawmakers appear to be asking the same questions:

"Despite the long history of this device, only recently has the FDA put out guidance that the use of laparoscopic power morcellators increases the risk of spreading unsuspected cancers in women to as high as 1 in 352 cases," they wrote in the letter to GAO. "As of the date of this letter, the morcellator remains on the market.

"It is unclear exactly how many women may be dead as a result of an unsuspected cancer having been spread by this device. FDA's warning came decades after some studies were already pointing to a serious problem.

"Despite these studies, as late as last year, the FDA, the medical device industry, and many gynecologists pointed to the risk of a hidden cancer as being low, only one-in-10,000.

"How did they get it wrong for so long?

"In light of these concerns we respectfully request you investigate the root cause failure that ultimately led to the FDA's black box warning on the use of laparoscopic power morcellators in Nov. 2014—over two decades after it was first approved."

The legislators asked GAO to consider four questions:

1. Did the FDA's reliance on the 510(k) approval policies and procedures sufficiently identify risks of adverse events before the laparoscopic power morcellator was allowed to enter the market?

2. Were the medical device reporting regulations (21 CFR 803) appropriately followed to protect patient safety in the case of the laparoscopic power morcellator by manufacturers, importers, user facilities, and the FDA?

3. What activities or training did manufacturers provide to clinicians and what professional society standards, if any, apply to training on the use of these devices?

4. What steps is the FDA taking after issuing the black box warning to further determine whether the laparoscopic power morcellator is safe to remain on the market?

The work requested by the members of Congress falls within the scope of GAO authority, a GAO spokesperson said to the Wall Street Journal. The investigation should begin in about five months, and FDA has agreed to cooperate.

The Congressional letter to the GAO can be found here.

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*Obituary*

## Gianni Bonadonna, 81, Pioneering Cancer Researcher

Gianni Bonadonna, 81, a pioneering cancer researcher whose work focused on Hodgkin's lymphoma and breast cancer, died Sept. 7.

His death was announced by the Istituto Nazionale Tumori of Milan.

Bonadonna research included the initial studies on the clinical efficacy of adriamycin (doxorubicin), epirubicin and bleomycin; a number of seminal trials on adjuvant and primary chemotherapy for high-risk breast cancer; as well as a combined modality for the treatment of Hodgkin's disease—in 1972, he designed a new combination of drugs known as ABVD: adriamycin, bleomycin, vinblastine and dacarbazine.

In 1973, he designed and conducted the first clinical trial to evaluate the efficacy of the combination CMF (cyclophosphamide, methotrexate and fluorouracil) as postoperative adjuvant treatment for breast carcinomas at a high risk of relapse.

Bonadonna was born in Milan in 1934. He received his medical degree from the University of Milano in 1959. He did his fellowship at Memorial Sloan Kettering Cancer Center from 1961 to 1964.

He then joined the Istituto Nazionale Tumori, where he became director of the Division of Medical Oncology in 1976. In 1991, he was appointed head of the Department of Cancer Medicine in the same institution and associate professor at the School of Hematology of the University in Milan. Since 1999, he has been founder and president of the Fondazione Michelangelo.

As a visiting professor in several universities all over the world, Bonadonna received numerous awards, including the Laurea Honoris Causae in Medicine from University of Torino; the Medal of Honor from the American Cancer Society; the Distinguished Service Award for Scientific Achievement and the David Karnofsky award from the American Society of Clinical Oncology; and the Federation of European Cancer Societies' Clinical Research Award.

As a tribute to his contributions in the field of breast cancer research, ASCO instituted the Gianni Bonadonna Breast Cancer Award and Lecture in 2007; presented annually to a researcher of merit in the field of breast cancer.

And in recognition of his research in Hodgkin's lymphomas, the Committee of the International Symposium on Hodgkin's lymphoma in Cologne officially instituted the Gianni Bonadonna Hodgkin's Disease Award and Lecture.

He is the author of over 550 publications in the clinical oncology field and of books on medicine for lay people and of one book on the Sepoy Revolution in India.

## CVS Marks First Anniversary Of Stopping Tobacco Sales

CVS Health marked the first anniversary of ending tobacco sales at its CVS/pharmacy locations, and released study data showing a reduction in cigarette purchases over the past year.

The company also announced a joint initiative between CVS Health and Scholastic to launch a school-based tobacco-prevention program.

The study, conducted by the CVS Health Research Institute, evaluated cigarette pack purchases at drug, food, big box, dollar, convenience and gas station retailers in the eight months after CVS/pharmacy stopped selling tobacco products.

The study found an additional one percent reduction in cigarette pack sales in states where CVS/pharmacy had a 15 percent or greater share of the retail pharmacy market, compared to states with no CVS/pharmacy stores. Over the same eight-month period, the average smoker in these states purchased five fewer cigarette packs and, in total, approximately 95 million fewer packs were sold.

The study also showed a four percent increase in nicotine patch purchases in the states with a CVS/pharmacy market share of 15 percent of more, in the period immediately following the end of tobacco sales.

"Over the last year, CVS Health has created partnerships with community organizations across the country that are dedicated to helping people quit smoking and communicating the importance of never starting tobacco use," said Eileen Howard Boone, senior vice president of corporate social responsibility and philanthropy at CVS Health, and president of the CVS Health Foundation.

"Today, we are proud to mark our one-year anniversary by building on our commitment to be a meaningful part of the effort to make the next generation tobacco-free. By partnering with an expert in education to launch this new program, we will reach millions of kids across the country with critical tobacco-prevention education."

The program will reach nearly three million children in the third, fourth and fifth grades when it

begins this fall, with a second component offered in some pilot markets for young adults in grades six and seven to be introduced in early 2016.

It will include classroom resources for teachers and students as well as take-home components that give parents the opportunity to talk to their children about smoking. The middle school component will include a student engagement program, with the chance to receive incentives such as scholarships and youth-focused community training.

## 70th Annual Lasker Awards Go To Witkin, Elledge, Allison, Medecins Sans Frontieres

The 70th annual Lasker Awards went to: Evelyn Witkin and Stephen Elledge for basic medical research; James Allison for clinical research; and Medecins Sans Frontieres for public service.

The awards carry an honorarium of $250,000 for each category, and will be presented Sept. 18 in New York City.

Witkin and Elledge received the 2015 Albert Lasker Basic Medical Research Award for their research illuminating the fundamentals of the DNA-damage response mechanism that protects the genome of all living organisms.

Witkin is a professor emerita at Rutgers University, and is a member of the National Academy of Sciences, a fellow of the American Association for the Advancement of Science, and the American Academy of Arts and Sciences. She has also received the Thomas Hunt Morgan Medal of the Genetics Society of America, the Wiley Prize in Biomedical Sciences and the National Medal of Science, presented to her by President George W. Bush in 2003.

Elledge is the Gregor Mendel Professor of Genetics and of Medicine at Harvard Medical School and Brigham and Women's Hospital. He is a member of the National Academy of Sciences and has been a Howard Hughes Medical Institute investigator since 1993. He has received the Lewis S. Rosenstiel Award for Distinguished Work in Basic Medical Research, Dickson Prize in Medicine from the University of Pittsburgh, the National Academy of Sciences Award in Molecular Biology, and the Paul Marks Prize for Cancer Research from Memorial Sloan Kettering Cancer Center, among others.

Witkin and Elledge received the award for laying the conceptual and experimental foundation that led to our understanding of the intricately organized systems that ensure genetic fidelity and safeguard organismal vitality. Witkin figured out that bacteria respond to DNA damage by triggering multiple protective physiological activities. Elledge detailed the molecular pathway by which cells in more complex organisms, including humans, detect and respond to deviant DNA structures.

Allison received the 2015 Lasker~DeBakey Clinical Medical Research Award for the discovery and development of monoclonal antibody therapy that unleashes T cells to fight cancer.

Allison, of MD Anderson Cancer Center, is a fellow in the American Academy of Microbiology, has previously been awarded the Breakthrough Prize in Life Sciences, the Lloyd J.Old Award in Cancer Immunology from AACR-CRI, and the Richard V. Smalley, MD Memorial Lectureship Award by the International Society for Biological Therapy of Cancer.

In the mid-90s, Allison and other scientists showed that a protein called CTLA-4 subdues T-cell activation. While some proteins enflame the immune cells, CTLA-4 reins in a response that might otherwise cause overzealous reactions and autoimmune damage. By suppressing CTLA-4 blocks, Allison was able to unleash the T cells of the immune system to fight tumors.

The findings from this research resulted in new treatments that prolonged by more than a decade the lives of hundreds of patients with metastatic melanoma, which otherwise kills 50 percent of patients in less than a year.

Medecins Sans Frontieres, or Doctors Without Borders, received the 2015 Lasker~Bloomberg Public Service Award for its frontline responses to the recent Ebola outbreak in Africa.

"Medecins Sans Frontieres took the lead in responding to the Ebola disaster while others sat on the sidelines," said Alfred Sommer, Johns Hopkins Bloomberg School of Public Health, and chair of the Lasker Foundation's Public Service Award jury. "MSF showed remarkable leadership in combating a major health crisis. They set up facilities and procedures to contain the outbreak, trained local health workers, and urged international governments to take this outbreak seriously."

Since the beginning of the most recent Ebola outbreak in West Africa in March 2014, more than 11,000 people lost their lives, including hundreds of health workers. MSF sent experts, built hospitals, imported necessary supplies, and set up systems to

receive and treat patients.

In May, the World Health Organization and its constituent countries announced that it would create a $100M fund that will support an international rapid response system for future outbreaks.

"This year's Laureates have opened up new frontiers into genetic processes essential to all life; developed novel cancer therapies that unleash the immune system; and worked with great dedication to contain a devastating Ebola epidemic," said Claire Pomeroy, president of the Lasker Foundation. "They remind us all that investing in biological sciences and medical research is crucial for our future."

*In Brief*

## Mirkin Awarded Sackler Prize By National Academy of Sciences

(Continued from page 1)

Mirkin is a professor at Northwestern University and director of its International Institute for Nanotechnology.

He was awarded the $400,000 prize "for impressively integrating chemistry, materials science, molecular biology, and biomedicine in the development of spherical nucleic acids that are widely used in the rapid and automated diagnosis of infectious diseases and many other human diseases—including cancers and cardiac disease—and in the detection of drug-resistant bacteria." Mirkin will receive two-thirds of the prize money; the remaining third will support his research at Northwestern.

The prize will be presented Oct. 13 at the National Academy of Sciences building in Washington, D.C.

The annual prize was established through a gift from Raymond and Beverly Sackler and their foundation to recognize significant advances in convergence research, the integration of two or more of the following disciplines: mathematics, physics, chemistry, biomedicine, biology, astronomy, earth sciences, engineering, and computational science.

"By successfully combining the power of many scientific disciplines, Chad Mirkin created an entirely new kind of nucleic acid that is fueling critical advances in the diagnosis and treatment of devastating illnesses," said National Academy of Sciences President Ralph Cicerone. "We are pleased to recognize his significant achievements in convergence research with this prize."

Mirkin is the George B. Rathmann Professor of Chemistry and professor of medicine, chemical and biological engineering, biomedical engineering, and materials science at Northwestern University. A member of the National Academy of Sciences, the National Academy of Engineering, and the National Academy of Medicine, he is the recipient of more than 100 national and international awards. Mirkin also serves on the President's Council of Advisors on Science and Technology.

**CARLOS ARTEAGA** and **FREDERICK ALT** were named the winners of the 2015 Prize for Scientific Excellence by the **American-Italian Cancer Foundation.**

Arteaga is the Donna S. Hall Professor of Breast Cancer and director of the Center for Cancer Targeted Therapies and the Breast Cancer Program at Vanderbilt-Ingram Cancer Center, and recently completed a year as president of the American Association for Cancer Research. Arteaga was named a fellow of the AACR Academy earlier this year.

Alt is a Howard Hughes Medical Institute Investigator and director of the Program in Cellular and Molecular Medicine at Boston Children's Hospital, as well as the Charles A. Janeway Professor of Pediatrics and professor of genetics at Harvard Medical School.

They will receive the award at the 35th Annual AICF Benefit Dinner, Nov. 10 in New York City. The next day, a research symposium will be held at Memorial Sloan Kettering Cancer Center where each of the awardees will give a presentation on their work.

**HERBERT FRITSCHE** received the 2015 Abbott Award from the **International Society of Oncology and Biomarkers** for contributions to the field of basic or clinical oncology.

Fritsche is the lab director of Vermillion Inc.'s wholly owned subsidiary, ASPiRA LABS. He will receive the award Oct. 5 in Zakopane, Poland.

Prior to ASPiRA LABS, Fritsche was a professor of biochemistry and clinical chemistry section chief at MD Anderson Cancer Center.

**TROVAGENE INC.** established the **Trovagene Research Institute**, a European subsidiary focused on expanding the capabilities and adoption of the company's Precision Cancer Monitoring platform. Trovagene has also entered into a collaboration with the Department of Oncology at the University of Torino.

Alberto Bardelli will serve as the scientific chair of TRI. Bardelli, currently affiliated with the Department of Oncology at Torino Medical School and the Candiolo Cancer Institute in Italy, was among the

first to identify mutations in the kinase genes associated with colorectal cancer and other malignancies while at Johns Hopkins University.

He has authored or co-authored over 140 published papers, including his team's most recent publication in Nature Medicine, entitled "Clonal evolution and resistance to EGFR blockade in the blood of colorectal cancer patients."

The collaboration plans to pursue urine as a specimen for the detection and monitoring of oncogenic mutations.

*Drugs and Targets*

## FDA Grants Priority Review To Alectinib in Lung Cancer

**FDA granted Priority Review for alectinib,** an oral investigational anaplastic lymphoma kinase inhibitor, for the treatment of people with ALK-positive, locally advanced or metastatic non-small cell lung cancer who have progressed on or are intolerant to crizotinib.

Alectinib, sponsored by Genentech, was granted Breakthrough Therapy Designation by the FDA in June 2013 for people with ALK-positive NSCLC whose disease progressed on crizotinib.

The New Drug Application for alectinib includes data from two phase II studies, and the FDA will make a decision on approval by March 4, 2016.

ALEX, an ongoing, global randomized phase III study, is comparing alectinib to crizotinib as an initial treatment for people with advanced NSCLC whose tumors were characterized as ALK-positive by a companion immunohistochemistry test developed by Roche Diagnostics.

Results from the two phase II studies, NP28761 and NP28673, were recently presented at the 2015 Annual Meeting of the American Society of Clinical Oncology.

**Janssen Biotech Inc. announced an exclusive, worldwide license agreement with Alligator Bioscience AB** for ADC-1013, an immuno-oncology agent currently in phase I clinical studies.

Under terms of the agreement, Janssen will attain rights to develop and commercialize ADC-1013, an agonistic fully human monoclonal antibody. ADC-1013 targets CD40, an immuno-stimulatory receptor found on antigen-presenting cells such as dendritic cells. Stimulating this receptor initiates a process leading to an increase in T cells attacking a tumor.

Alligator Bioscience will receive an upfront payment plus additional milestone payments contingent upon reaching certain pre-determined development, regulatory and commercial milestones. Alligator Bioscience will complete the current phase I dose escalation study and Janssen will be responsible for all subsequent development of ADC-1013, including research, development, manufacturing, regulatory and commercialization activities.

**Sequenom Inc. entered into a clinical research collaboration with the University of California, San Diego** Moores Cancer Center to explore the utility of Sequenom's new liquid biopsy assay to comprehensively profile circulating cell-free tumor DNA in blood to enable serial monitoring and assist with therapy selection in cancer patients.

"Sequenom has designed a comprehensive multi-gene panel based on the clinical actionability of cancer genes. The ability to match patients to a growing list of treatments and to monitor their response by a simple blood draw promises to make a significant difference in the way we treat cancer patients at UC San Diego," said Razelle Kurzrock, chief of the Division of Hematology & Oncology and Murray Professor of Medicine, senior deputy director of Clinical Science and director of the Center for Personalized Cancer Therapy & Clinical Trials Office.

Sequenom is currently developing a Research Use Only assay with an initial focus on the detection and molecular profiling of late stage non-hematologic malignancies, where tissue biopsies are not available or too risky to obtain.

The assay will cover a breadth of cancer types by analyzing over 100 cancer-related genes that are associated with a FDA-approved drug treatment, included in professional society guidelines, linked to targeted therapies currently in clinical trials, or part of well-documented cancer pathways.

**Vaccinogen Inc. entered into an agreement with Dublin City University**, through one of its subsidiaries, to provide an exclusive two-year option to evaluate and acquire a high-throughput, multiplex, analysis platform, DiCAST.

In conjunction with the agreement, the scientific team that developed DiCAST, including lead inventor Paul Leonard, has joined Vaccinogen, and will spearhead the company's operations in Ireland.

Vaccinogen intends to utilize DiCAST to expand and significantly accelerate the its human monoclonal

antibody program, screening patient-derived biological samples acquired after gaining anti-cancer immunity. Vaccinogen plans to utilize DiCAST to identify immunologically relevant data from the biological samples to develop the next generation of safe and effective cancer vaccines and immunotherapies.

If Vaccinogen elects to exercise its option to acquire DiCAST, the technology may be further developed beyond Vaccinogen's initial antibody focus to other biologic and small molecule drug discovery, with potential use across multiple areas of therapeutics, diagnostics, and basic research.

DiCAST (Direct Clone Analysis and Selection Technology) is a novel, patent pending technology designed to improve the speed and quality of early-stage drug discovery. This preclinical platform allows for simultaneous analysis of millions of samples to determine immunologic activity and identify optimal targets for further development.

The DiCAST platform includes three specialized components: a densely packed microcapillary array, real-time assay visualization with proprietary convergent computation software integrating multiple analytical datasets, and a novel custom-built high precision recovery system that allows for individual target acquisition while preserving biological material integrity.

Laboratory results have demonstrated that DiCAST can analyze over 35,000 times more samples per test iteration than traditional methods and can identify new immunological components with improved performance that previously could not be identified using traditional approaches.

The financial terms of the option agreement were not disclosed.

**The Ontario Institute for Cancer Research and the Structural Genomics Consortium in Toronto** developed a new drug prototype, called OICR-9429, and made it freely available to the research community.

Research conducted by international groups using OICR-9429 has shown it to be effective in stopping cancer cell growth in breast cancer cell lines and a specific subtype of leukemia cells. OICR-9429 works to inhibit a protein called WDR5, and independent studies from Philadelphia and Vienna have now shown that the cellular target of OICR-9429 may be relevant for drug discovery, according to the institute.

"In the time that it would normally take to negotiate a legal agreement to provide OICR-9429 to other research teams we have received results back from our collaborators showing that it can kill two different types of cancer cells," said Cheryl Arrowsmith, chief scientist at SGC Toronto. "Opening our chemistry capabilities to the world's scientists allowed us to crowdsource and accelerate the research."

Arrowsmith is also a professor in the Department of Medical Biophysics at the University of Toronto and a senior scientist at Princess Margaret Cancer Centre.

A study led by Shelly Berger at the University of Pennsylvania used OICR-9429 to stop cancer cell growth in a panel of breast cancer cell lines driven by mutated forms of the gene p53. In its normal form, p53 is a tumor-suppressor, however once it is mutated it leads to a gain of function, and causes cancers to grow though its stimulation of WDR5 function. This research is significant as p53 is mutated in at least half of all cancers and is dysregulated in others.

A team headed by Florian Grebien and Giulio Superti-Furga at the CeMM Research Center for Molecular Medicine in Vienna, Austria used OICR-9429 to demonstrate the potential of WDR5 as a therapeutic target for leukemia.

Their research showed that OICR-9429 stopped the growth of leukemia cells with a very specific mutation found in about nine per cent of patients with acute myeloid leukemia.

These two studies culminated in joint publications, in Nature and Nature Chemical Biology respectively, between the international researchers and the Ontario-based OICR and SGC teams.

**Today, 836 medicines and vaccines are in development** for cancer by U.S. biopharmaceutical companies—all of which are either in clinical trials or awaiting review by the FDA—according to a report from the Pharmaceutical Research and Manufacturers of America.

This includes 123 therapies for lung cancer; 106 for several types of leukemia; 92 for lymphoma, including non-Hodgkin lymphoma; 82 for breast cancer; 58 for brain tumors; and 53 for skin cancer, including melanoma.

Approximately 80 percent of these cancer drugs are potentially first-in-class medicines, and 73 percent have the potential to be personalized medicines, according to the report, Medicines in Development 2015.

The full list of medicines, sponsors and indications can be found here.