# THE CANCER LETTER

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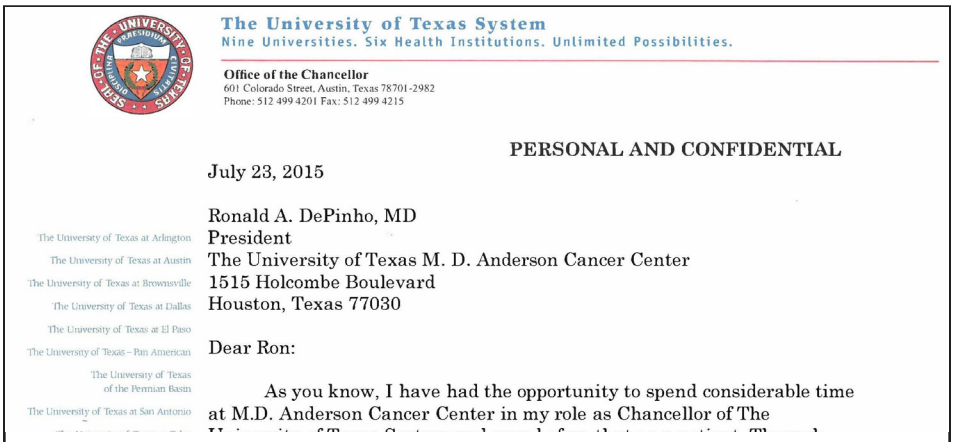

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Phone: 512 499 4201 Fax: 512 499 4215

PERSONAL AND CONFIDENTIAL

July 23, 2015

Ronald A. DePinho, MD
President
The University of Texas M. D. Anderson Cancer Center
1515 Holcombe Boulevard
Houston, Texas 77030

The University of Texas at Arlington
The University of Texas at Austin
The University of Texas at Brownsville
The University of Texas at Dallas
The University of Texas at El Paso
The University of Texas – Pan American
The University of Texas of the Permian Basin
The University of Texas at San Antonio

Dear Ron:

As you know, I have had the opportunity to spend considerable time at M.D. Anderson Cancer Center in my role as Chancellor of The

## UT Chancellor Mandates Unprecedented Shared Governance Structure at MD Anderson

*By Matthew Bin Han Ong and Conor Hale*

After years of turmoil and plunging morale at MD Anderson Cancer Center, the UT System took what observers describe as an unprecedented step—forming a Shared Governance Committee.

The new structure, instituted Sept. 1, disbands the once powerful Executive Committee, thereby changing the cancer center's top-down power structure.

The new governance committee is designed to incorporate input from the faculty, and serve as the top advisory body to the institution's president, Ronald DePinho.

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*Editorial*

## Judge: Amgen Can't Depose Cancer Letter Reporter (Me)

*By Paul Goldberg*

A federal judge ruled that Amgen Inc. cannot force me to answer questions related to a 2007 story that sparked a class action suit by investors and triggered a change in FDA regulations of erythropoiesis-stimulating agents.

Judge Amit Mehta, of the U.S. District Court for the District of Columbia, quashed a subpoena filed by Amgen that sought information related to my reporting of a story about a critically important clinical trial showing that patients who received Aranesp did worse than patients who did not.

(Continued to page 6)

*In Brief*

## Edith Mitchell Named President of NMA

**EDITH MITCHELL** was named president of the **National Medical Association**, at the organization's 113th annual convention and scientific assembly in Detroit Aug 4. Mitchell is a professor of medical oncology at Thomas Jefferson University.

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# UT System Chancellor Mandates Shared Governance at MD Anderson

(Continued from page 1)

The group will include all MD Anderson division heads, the chair of the Faculty Senate, as well as the chair-elect, the immediate past chair, and senior executives of the Senate. The decision was announced Aug. 14, in a faculty-wide email from DePinho and Gary Whitman, chair of the Faculty Senate.

"In recent months, we have focused intensely on bringing together voices and talents from across our 21,000-employee institution to ensure adequate leadership representation and to enable awareness of issues and ideas that can lead to, or detract from, MD Anderson's greatness," the email said.

The email included two letters sent by UT System Chancellor Bill McRaven, addressed to DePinho and the Faculty Senate Executive Committee, respectively.

"The single most important issue, in my opinion, is assuring that bidirectional trust flourishes within the MD Anderson family," McRaven wrote to DePinho in a letter that was dated July 22, but released Aug. 14. "Toward that end, I believe that a new shared governance structure will be transformative."

McRaven's approach is highly unusual, observers say.

"There have been occasions, hardly common, but not exceedingly rare, in which members of the governing board have suggested/advised/urged/insisted that an autocratic administration provide/allow the faculty a stronger role in academic governance," Jordan Kurland, associate general secretary at the American Association of University Professors, said in an email to The Cancer Letter. "If the object of the board's or system's concern is expected to remain in office, however, this pressure is applied privately.

"I'm not aware of any case like that currently at MD Anderson, where the system chancellor has approached it as a matter of public concern," said Kurland, who has been with AAUP for about 50 years.

McRaven's letter describes how the new Shared Governance Committee should operate—including which issues it should cover and how frequently the members should meet.

McRaven also instructed MD Anderson's leadership to develop an internal communication plan that would make the committee's decision-making into a transparent process, "especially in terms of how clinical revenues are directed."

"The shared governance team will serve in an advisory capacity to the President, who will continue to operate as the final decision authority for the institution," McRaven wrote. "At the same time, the shared governance team includes broad representation of the institution, and if governance is functioning effectively, with thorough discussion, deliberation and opportunity for dissent, the decisions of the President will be closely aligned with the recommendations of the shared governance committee.

"Once the decision is made by the President, it will be considered final."

In the letter, McRaven expressed his "full, unqualified, and unwavering support" for DePinho and his leadership, also saying that his "many conversations with faculty and staff reveal that there is a continuing sense that more can be done."

"It is my goal, therefore, to communicate a set of institutional priorities that I hope will be embraced not only by your executive and faculty leadership team, but also by the faculty and the administrators," he wrote.

The new shared governance structure is an MD Anderson effort, DePinho's administration officials said.

"The Shared Governance Committee is the result of extensive work by faculty leaders and administrators, all of whom are committed to fostering a collaborative spirit, building on our strong institutional momentum, seizing extraordinary scientific opportunities and wisely addressing critical challenges facing health care," MD Anderson said in a statement to The Cancer Letter.

"It's clear our strides toward shared governance and responsibility in recent years have proved successful based on the exceptional success of the institution on all fronts—academic, clinical, scientific, fiscal, philanthropic and recruitment.

**Editor & Publisher**: Paul Goldberg
**Associate Editor**: Conor Hale
**Reporter**: Matthew Bin Han Ong

Editorial, Subscriptions and Customer Service:
202-362-1809 Fax: 202-379-1787
PO Box 9905, Washington DC 20016
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"Our recently closed fiscal year 2015 was one of our best ever in all of these areas. Together, we are moving toward our shared mission to reduce the pain and suffering of cancer globally.

"MD Anderson is committed to providing fair and competitive compensation for all positions based on market data. In addition to market data, the institution will continue to consider the specific responsibilities and expectations for each position. This is not only sound management, but also is consistent with the policies of the University of Texas System."

MD Anderson recently proposed pay raises to members of the Executive Committee (The Cancer Letter, April 17). It is not publicly known whether MD Anderson will freeze or roll back compensation for executive leaders, as the faculty proposed in a white paper presented to McRaven June 14 (The Cancer Letter, July 13).

**"I am Not Aware of Anything Quite so Thoughtful and Engaged"**

A directive placing faculty officers on an institution-wide executive committee is unheard of, said Matthew Finkin, director of the Program in Comparative Labor and Employment Law & Policy, and the Albert J. Harno and Edward W. Cleary Chair in Law at the University of Illinois.

"On its face the chancellor's initiative is most impressive: it takes shared governance seriously; it sets out key areas for improvement; it calls for transparency and accountability in achieving its goals," said Finkin, who has participated in four AAUP investigations and chaired two. "I am not aware of anything quite so thoughtful and engaged."

Finkin is the author of two definitive books on tenure in the U.S.: The Case for Tenure, and For the Common Good: Principles of American Academic Freedom. He is also an author of Labor Law, a leading casebook in American legal education.

"This is really an amazing turn around. I am really curious to learn of the faculty's input in getting to this point and its reaction to what has, in effect, been ordered to be put in place," Finkin said.

**McRaven Calls for Team Effort**

McRaven thanked the Faculty Senate Executive Committee for its work—specifically the white paper the committee prepared in July, which addressed what it called "pervasive" low morale at the institution, and called for the UT System to freeze the salaries of DePinho and his executive team until they reach parity with faculty compensation (The Cancer Letter, July 13).

"As we look to the future, it is clear that a team effort will be required to improve the climate at MD Anderson," McRaven wrote in his letter to the Executive Committee. "The executive leadership team must embrace the principles of shared governance, transparency, and support of faculty academic effort. At the same time, the faculty must be an engaged and willing partner in these efforts."

McRaven also said MD Anderson must "overcome a historical misperception that the purpose of the Faculty Senate is to serve as the loyal opposition to the administration."

"The white paper has begun to change that dynamic—I have witnessed a genuine alignment of interests across the various stakeholder groups," McRaven wrote. "In the proposed new shared governance model, it will be key for all of those involved in decision-making roles to act first and foremost in the interests of the greater good of the institution."

Again calling for greater communication between all parties, McRaven wrote: "In my discussions with various stakeholders, it is clear that all constituents believe that internal communications can be improved at MD Anderson Cancer Center.

"Clearly, the executive leadership team understands that they have to do a better job in that regard, but I would also charge the Faculty Senate representatives to meet regularly with their constituents in order to make sure that they fully appreciate the range of opinions that are held. The white paper process illustrated that faculty opinion is diverse, and to be effective, the Faculty Senate cannot be seen as representing only one segment of the broad range of opinion.

"When meeting with faculty colleagues, it would be helpful if the message from the Faculty Senate representatives was as balanced as possible."

**Tenure and Evaluations**

In his letter to DePinho, McRaven noted concerns over the institution's policies on tenure and faculty evaluations.

In June, the American Association of University Professors censured MD Anderson after a yearlong feud over the decision to deny tenure to Kapil Mehta and Zhengxin Wang, two professors who had been unanimously recommended for tenure renewal by the MD Anderson Promotion and Tenure Committee (The Cancer Letter, June 13).

"The process of building trust will be advanced if faculty members feel that they have input into the process of evaluating the performance of all faculty

**2012 - 2015 Compensation for MD Anderson Leadership**

| Name | Title | *2015 Max. Projected Compensation | 2014 Total Direct Compensation | 2013 Total Direct Compensation | 2012 Total Direct Compensation |
|---|---|---|---|---|---|
| Ronald DePinho | President, Professor | $1,890,446 | $1,890,446 | $1,845,200 | $1,801,065 |
| Leon Leach | Executive Vice President | $1,606,434 | $1,553,860 | $1,468,169 | $1,438,403 |
| Thomas Buchholz | Physician-in-Chief, EVP | $1,350,108 | $1,027,233 | $1,000,932 | $854,255 |
| Ethan Dmitrovsky | Provost, EVP | $1,346,356 | $1,095,174 | $160,016 | $0 |
| Robert Fontaine | Executive Chief of Staff | $1,390,964 | $1,293,935 | $1,222,397 | $794,984 |
| Thomas Burke | EVP, MDA Cancer Network | $1,573,366 | $1,523,928 | $1,442,632 | $1,430,189 |

*Source: The Higher Education Administrative Accountability Report (Special Provisions, Sec. 5 FY 2015)

administrators," McRaven wrote, discussing the upward evaluation process.

"The faculty administrator upward evaluation process was not implemented since 2010, in part because it was perceived that it was not functioning in a way that provided constructive feedback to faculty upper administrators. That may well have been a justified decision at the time, but the passage of five years without faculty input into faculty administrator evaluations is adding to the sense that faculty do not have an adequate voice in the organization."

McRaven called for a summary report of the faculty reviews for promotions and tenure as well as actions taken over the previous appointment cycle:

"During the past year, one of the issues that was addressed was a perception that there is an inadequate appeals process for rejections of promotion and tenure requests. A proposal was implemented to create an advisory review to the President when he or she disagrees with a unanimous favorable vote of the promotion and tenure committee.

"Thus far, there has not been a need to invoke this new process, so it is premature to judge whether or not it is working. Therefore, I look forward to a summary report from the 2014-15 annual appointment cycle concerning the number of faculty reviewed in the promotion and tenure process, the distribution of votes by the promotion and tenure committee, and the need, if any, to invoke the appeals process. I trust that the review of these data over time will reveal whether the new grievance process is working or if it requires further modification.

"Faculty grievances also arise outside of the promotion and tenure process and it is appropriate for the shared governance committee to charge a group of faculty and administrators to conduct a review of the current faculty grievance appeals mechanisms and make recommendations about improvements in the policies and procedures. Recommendations for changes in grievance policies and procedures should be submitted to the shared governance committee and those that are endorsed should be transmitted to the President to render a final decision. Once implemented, these policies and procedures should be monitored over time to assure that they are working effectively."

**Justifiable Salaries?**

Top administrators at MD Anderson earn seven-figure salaries, and their compensation has been increasing dramatically while faculty raises have been slow (The Cancer Letter, April 17).

In 2014, basic science faculty members received an incentive payment of $2,000. Incentive pay for clinical staff was calculated as a percentage of base pay linked to the amount of their work in clinical operations and other factors, officials said. There was no merit raise in 2014, because MD Anderson didn't meet the institutional financial goal required to trigger that merit pay, officials said.

In fiscal year 2015, faculty members received 4 percent merit raises, based on performance in the FY2014 fiscal year. The budget for fiscal 2016 includes a 3 percent merit increase for faculty as well as an incentive program, which is in the midst of being updated, according to slides presented to the center's Budget Advisory Committee April 6. The document is posted here.

Two top administrators at MD Anderson Cancer Center, whose job responsibilities include maintaining harmony with the faculty, received substantial pay increases for having "excelled beyond expectation" and "effectively" directing the center's clinical activities.

According to documents obtained by The Cancer Letter under the Texas Public Information Act, MD

Anderson Provost Ethan Dmitrovsky and Physician-in-Chief Thomas Buchholz received $200,000 each in deferred compensation in 2015.

With incentive pay, supplemental annuity and deferred compensation included, the 2015 raise could boost Dmitrovsky's total paycheck by as much as 22.9 percent compared to fiscal 2014. Buchholz's compensation could increase by 31.4 percent.

In 2014, with bonuses and incentive pay, Dmitrovsky's W-2 form reported that he earned $1,095,174 from MD Anderson. Buchholz's W-2 reported his earnings at $1,027,233 last year.

However, compensation for the two executives was "not at equity with other members of our executive leadership team, particularly with regard to deferred compensation offerings," MD Anderson President Ronald DePinho wrote to the Board of Regents.

Leonard Zwelling, a medical oncologist and former vice president for research administration at MD Anderson, argues that the cancer center is paying its executives too much.

"The question is, are these salaries really justified?" Zwelling wrote on his blog. "The new President of UT Austin turned down $1M for what he thought was a more appropriate $750,000 and he's running a huge campus that dwarfs MD Anderson's in size (but probably not clinical revenue).

"Then we heard that the reason that Buchholz and Dmitrovsky needed to make more is because they were assuming some of the work the President had been doing. Well, The Ronald's salary was not reduced in sync with his right and left hand men's increases and what is that work the two picked up anyway?

"Now, with the new shared governance, some of the pressure ought to be off the Physician-in-Chief and Provost as the faculty are there to prop them up (I wonder if the new faculty members of Leadership team will get raises, too).

"Perhaps it is time to bring in the auditors from the state to assess the value of the Leadership Team folks to the institution, compare their pay with that of the faculty both at Anderson and throughout the UT System, and then compare their pay with that of similarly-titled colleagues at other cancer centers adjusted for geographical inflation. (It costs about 40% more to live in New York City than in Houston, so a dollar for dollar comparison with personnel at Memorial Sloan Kettering is ridiculous)."

MD Anderson officials didn't respond to The Cancer Letter's questions about compensation for members of the former Executive Committee.

**DePinho, Faculty Senate Announce Change**

In an email sent to MD Anderson faculty and staff Aug. 14, DePinho and Faculty Senate Chair Gary Whitman pledged to work cooperatively.

*The text of the email follows:*

Date: August 14, 2015
To: All MD Anderson Faculty
From: Ronald A. DePinho, M.D., President and Gary J. Whitman, M.D., Faculty Senate Chair

In recent months, we have focused intensely on bringing together voices and talents from across our 21,000-employee institution to ensure adequate leadership representation and to enable awareness of issues and ideas that can lead to, or detract from, MD Anderson's greatness. In addition, Chancellor Bill McRaven has provided sage advice in recent weeks and offered his perspectives and guidance in the form of two letters, addressed to both of us. We both wish to share these letters with you (see attached).

We are unified in our interest to advance the institution and are pleased to announce a new era of collaborative leadership at MD Anderson — marked by a genuine interest to create shared understanding and shared responsibility. To accelerate the realization of collaborative leadership, we are taking definitive steps to establish the institution's first Shared Governance Committee. Effective September 1, 2015, this committee will become MD Anderson's foremost advisory body to the president, assuming the responsibilities of the Executive Committee, which will be disbanded in its current form on August 31. Membership of the Shared Governance Committee will comprise all division heads; the Faculty Senate's immediate past chair, current chair and chair-elect; and senior executives.

A renewed spirit of cooperation, rooted in our mutual desire to make this the best institution it can be, is palpable. It has been a key element over the past several months in advancing our institutional strategic plan well into its current implementation phase; ensuring progress across key focus areas; developing solutions for emergent operational issues; and supporting and advancing our world-leading faculty and staff to enable their continued scientific and clinical achievements for the benefit of countless people across the globe. We want to foster this collaborative spirit, build on our strong institutional momentum, seize extraordinary scientific opportunities and address critical challenges facing healthcare.

In summary, our new Shared Governance

Committee has one fundamental objective: to collaboratively facilitate the advancement of MD Anderson toward achievement of our mission.

We are excited about working closely with each of you in Making Cancer History, together.

Ronald A. DePinho, M.D.
President
Gary J. Whitman, M.D.
Chair, Executive Committee of the Faculty Senate

*Editorial*

## Judge: Amgen Can't Depose Cancer Letter Reporter (Me)

(Continued from page 1)

The ruling, dated Aug. 21, is posted here.

Since I am a participant in these events, I have to call this story an editorial, which is just as well, because the rubric allows me to get a few things off my chest:

• As a member of the press and as a naturalized American, I consider it a privilege to defend our First Amendment rights against attacks from one of the world's largest biotechnology companies.

• Though much of discussion is about securities fraud, the real issue is harm done to patients, and Amgen's decision not to release information from a negative clinical trial. I am told that by reporting this story and directly triggering FDA action, I may have saved some lives. Reporters don't get to do this often. Stories like this one explain why we have the First Amendment.

Let's roll back the clock to the beginning:

On Feb. 16, 2007, I reported that Amgen failed to disclose the results of a study called DAHANCA 10 (insert link), which tested Aranesp in head and neck cancer patients in Denmark. The study was stopped, because patients who received Aranesp did worse than patients who didn't.

After my story was published, Amgen's stock crashed, precipitating a shareholders lawsuit. Sequelae included a congressional investigation, a hearing of the House Committee on Energy & Commerce, an investigation by the Securities and Exchange Commission, a Supreme Court ruling, and—most importantly—a decision by FDA to limit the use of red cell growth factors to treat chemotherapy-induced anemia. Books have been written about this controversy, including one with my name on the cover.

Defending the lawsuit filed by shareholders, Amgen lawyers formulated a novel argument. Wall Street analysts learned about the Danish study before my story was published, they contend.

While the plaintiffs argue that my story constituted a "corrective disclosure" of information to the market, Amgen lawyers say that my story was irrelevant. They argue that I had to have made the disclosures to Wall Street sources as I was trying to figure out the significance of the DAHANCA finding. In its filings, the company postulates that the key players learned about study from *me*, as I was doing my reporting.

Or at least this was Amgen's stated rationale for wanting to depose me.

Fortunately, this is America. When litigants in civil cases seek to depose reporters, they have to (1) show that the information they seek goes to the heart of the matter in the lawsuit, and (2) demonstrate that they had made a diligent effort to obtain information from alternative sources.

Compelling a reporter to testify should be a rare exception rather than the rule, Judge Mehta wrote in his excellent opinion. Amgen had failed to interview either the physicians who are cited as having been informed about the DAHANCA 10 results or to establish what Wall Street analysts may have known before the story was published.

Mehta writes:

"Amgen has failed to demonstrate the requisite diligence in seeking evidence from alternative sources. Amgen argues that it cannot reasonably be expected to depose a large quantity of 'securities analysts covering the biotechnology sector' in the hope of finding the two with whom Goldberg spoke. Unfortunately for Amgen, that is precisely what the law in this circuit requires.

"Here, Amgen knows of 25 or 26 analysts who followed the company at the time the DAHANCA 10 study was conducted. Deposing, at most, only three of them to discover which of them might have spoken to Goldberg and thus learned about the study before the Article's publication, is not enough. Deposing a large number of analysts in the hope of finding the two that spoke to Goldberg might indeed be akin to looking for a needle in a haystack, as Amgen contends. But the law requires Amgen to have conducted a thorough search of the hay before deposing Goldberg, which it failed to do."

Mehta also notes the company's failure to depose doctors who knew about the study.

One of them was Michael Henke, a German radiation therapist, who is quoted in my story stating that he found the Danish results on the Internet. Henke was one of the first clinical researchers to suggest that

these agents were harming head and neck cancer patients (The Cancer Letter, Oct. 24, 2003).

The second is Charles Bennett, an oncologist and a drug safety expert, whom I quoted stating that he heard about the results from a European colleague. Bennett would later publish a landmark study in JAMA (The Cancer Letter, June 1, 2007, Feb. 29, 2008), in which he points to harm from agents that include Aranesp.

"If confirming Dr. Bennett's pre-Article knowledge of the study is as critical as Amgen claims, it would have been a simple matter to serve him with a subpoena for testimony," Mehta wrote. "Instead, Amgen only served him with a document subpoena, which of course could not provide Amgen with the admissible testimonial evidence it seeks.

"Amgen also did not seek evidence from Dr. Henke. Admittedly, the burden with regard to Dr. Henke is far greater. As Dr. Henke is a resident of Germany, Amgen would have been required to proceed under The Hague Convention to secure evidence from him.

"But unfortunately for Amgen, there is no foreign evidence exception to the exhaustion requirement. Litigation in this case commenced at least two years ago and, in that time, Amgen has not made any effort to secure admissible evidence from Dr. Henke. Nor has it shown that obtaining evidence from Dr. Henke would be particularly burdensome or difficult to obtain under an international convention. A journalist's privilege should be overridden only as 'a last resort.' In the case of both Dr. Henke and Dr. Bennett, Amgen has failed to pursue evidence about their knowledge of the DAHANCA 10 study from the doctors themselves."

The company also neglected to depose the head of the DAHANCA group, Jens Overgaard, the DAHANCA 10 PI, the judge noted.

"Notably, Amgen has not sought discovery from the one person that might have information about how widespread knowledge was about the DAHANCA 10 study before the Article's publication—the study's principal investigator, Jens Overgaard. According to Amgen, it has concluded that Overgaard would have little to offer other than that the DAHANCA 10 study was posted on a website. If Amgen has concluded that Overgaard would have little to offer to show the market's knowledge of the study, it is hard to believe that Goldberg would be able to offer any more.

"Amgen has not shown how it expects to obtain critical evidence by asking Goldberg the open-ended question whether he spoke to anyone else who knew about the study before the Article's publication," Mehta wrote.

Anyone who read my 2007 story carefully would have been able to see that, even if compelled, even if water-boarded, there would be no way I would be able to do anything but express surprise at Amgen's theory that I had in effect disclosed to Wall Street that DAHANCA 10 came up negative.

I said in an affidavit that I spoke with two "Wall Street sources" whom I didn't name in the story—one whom I will never identify (as per agreement, not because of this person's prominence), and another, whose name I simply forgot. (Case No. 1:15-00825, Doc. 1-1, Exhibit A to Declaration of Paul Goldberg.)

I didn't need many sources. In an analogous hypothetical situation where a group of 25 people is basking in sunshine, you don't need to talk to all of them to ascertain that it's not raining.

What does Amgen actually want from me?

I am not prone to paranoid fantasies, and neither are my lawyers, who so ably represented me in this matter.

Steven Lieberman, The Cancer Letter's lead attorney who argued the case before Judge Mehta, said Amgen's actions have the smell of revenge.

"This is the case of a company with unlimited resources choosing to flout the legal system to punish the publication that outed them," said Lieberman, an attorney with Rothwell, Figg, Ernst & Manbeck."This ruling sends a message to corporations: no matter how rich and powerful you are, you can't flout the Constitution.

"Judge Mehta's excellent opinion explained that companies in litigation cannot simply use journalists as a regular part of the discovery process. They may do so only when they have undertaken the extensive alternative steps that the constitution requires of them."

Gregg Leslie, legal defense director of the Reporters Committee for Freedom of the Press, also praised the opinion: "This is a great decision, because we constantly see big corporations try to sweep up all information from reporters when they're engaged in litigation, as if journalists are just another research resource for them. Journalists need to function independently to keep good information and analysis flowing to the public, and this decision helps with that.

"It is particularly important to get a decision like this in a case involving a specialist publication that often doesn't have the resources of a big media company, but which is doing intensive research and reporting that must be protected," Leslie said to The Cancer Letter.

Companies that face class action suits from shareholders try to make litigation as expensive as possible for their adversaries. This is because attorneys for the plaintiffs get paid only if they win, and there is always a chance that they would be unable to continue

to invest in litigation.

In this case, which could be worth billions, Amgen dragged the plaintiffs all the way to the Supreme Court. The company challenged the certification of class, a crucial step in a class action suit, by a lower court.

Amgen argued that plaintiffs should have been required to prove materiality of Amgen's alleged misrepresentations and omissions before class certification in order to satisfy the requirement that "questions of law or fact common to class members predominate over any questions affecting only individual members."

An appellate court upheld the lower court's certification of a class action, and Amgen pressed on. Finally, on Feb. 27, 2013, the Supreme Court upheld the lower and appeals court rulings, finding Amgen's arguments "unpersuasive."

An excerpt from the Supreme Court decision follows:

"While Connecticut Retirement [the plaintiff in the case against Amgen] certainly must prove materiality to prevail on the merits, we hold that such proof is not a prerequisite to class certification. [Federal Rule of Civil Procedure] 23(b)(3) requires a showing that *questions* common to the class predominate, not that those questions will be answered, on the merits, in favor of the class.

"Because materiality is judged according to an objective standard, the materiality of Amgen's alleged misrepresentations and omissions is a question common to all members of the class Connecticut Retirement would represent. The alleged misrepresentations and omissions, whether material or immaterial, would be so equally for all investors composing the class. As vital, the plaintiff class's inability to prove materiality would not result in individual questions predominating. Instead, a failure of proof on the issue of materiality would end the case, given that materiality is an essential element of the class members' securities-fraud claims. As to materiality, therefore, the class is entirely cohesive: It will prevail or fail in unison. In no event will the individual circumstances of particular class members bear on the inquiry.

"Essentially, Amgen, also the dissenters from today's decision, would have us put the cart before the horse. To gain certification under Rule 23(b)(3), Amgen and the dissenters urge, Connecticut Retirement must first establish that it will win the fray. But the office of a Rule 23(b)(3) certification ruling is not to adjudicate the case; rather, it is to select the 'metho[d]' best suited to adjudication of the controversy 'fairly and efficiently.'"

**Results of Aggressive Promotion**

Amgen has faced multiple other legal problems related to promotion of Aranesp.

On Aug. 18, the company paid $71 million to resolve allegations that the biotech company unlawfully promoted biologic medications Aranesp and Enbrel for off-label uses. The Complaint and Consent Judgment filed today alleges that Amgen violated state consumer protection laws by:

(1) Promoting Aranesp for dosing frequencies longer than the FDA approved label without competent and reliable scientific evidence to substantiate the extended dosing frequencies;

(2) Promoting Aranesp for anemia caused by cancer without having FDA approval or competent and reliable scientific evidence to support it;

(3) Promoting Enbrel for mild plaque psoriasis even though Enbrel is only approved by the FDA to treat chronic moderate to severe plaque psoriasis; and

(4) Overstating the length of Enbrel's efficacy in treating plaque psoriasis. By obtaining a compendium listing (typically, a non-profit reference book listing a drug's strengths, qualities and ingredients) for Aranesp for anemia of cancer, Amgen unlawfully facilitated health care coverage and reimbursement for the drug.

"Pharmaceutical companies are prohibited from making unapproved and unsubstantiated claims about prescription drugs," New York State Attorney General Eric Schneiderman said in a statement. "Consumers need to have confidence in the accuracy of claims made by pharmaceutical companies."

The consent judgment requires Amgen to reform its marketing and promotional practices. Under the terms of the consent judgment, Amgen shall not:

• Make, or cause to be made, any written or oral claim that is false, misleading, or deceptive in promoting Enbrel, Aranesp or any Erythropoietin stimulating agent ("ESA"), a red blood cell stimulant in the same class as Aranesp;

• Represent that Enbrel, Aranesp or any ESA has any sponsorship, approval, characteristics, ingredients, uses, benefits, quantities, or qualities that it does not have;

• Use a compendium listing or publication to promote Enbrel, Aranesp or any ESA for an off-label use to a health care professional;

• Allow Amgen Marketing and Amgen Sales to initiate interactions with a compendium or determine the content of any materials for submissions to a compendium relating to Enbrel, Aranesp or any ESA; and

• Submit a special supplement to a compendium

to support an off-label use of Enbrel, Aranesp or any ESA or use a third party to lobby a compendium on Amgen's behalf without notifying the compendium that it is acting at Amgen's request.

States participating in the settlement are Alabama, Alaska, Arizona, Arkansas, California, Colorado, Connecticut, Delaware, District of Columbia, Florida, Georgia, Hawaii, Idaho, Illinois, Indiana, Iowa, Kansas, Kentucky, Louisiana, Maine, Maryland, Massachusetts, Michigan, Minnesota, Missouri, Montana, Nebraska, Nevada, New Hampshire, New Jersey, New Mexico, New York, North Carolina, North Dakota, Ohio, Oklahoma, Oregon, Pennsylvania, Rhode Island, South Dakota, Tennessee, Texas, Utah, Vermont, Virginia, Washington, West Virginia, Wisconsin, and Wyoming.

In October, 2011, Amgen paid $780 million to settle several criminal and civil investigations that accuse the company of using illegal sales and marketing practices in promoting the red-blood-cell building agents Aranesp and Epogen (The Cancer Letter, Oct. 28, 2011).

Most of the whistleblower lawsuits were sealed, but one lawsuit that was made available was filed by Kassie Westmoreland, a former Amgen sales representative and Aranesp product manager.

That lawsuit was joined by 18 state-level attorneys general. The lawsuit accuses Amgen of placing excessive amounts of Aranesp into containers and, as part of their marketing, told healthcare providers that they could sell the excess medication and profit from the sale. The complaint alleges that Amgen overfilled Aranesp to compete with Procrit, a rival drug. According to court documents, the overfill in Aranesp prescriptions was higher than those of Procrit.

Though Procrit is marketed by Johnson & Johnson, it's produced in the U.S. by Amgen. The lawsuit was filed in late 2009 (The Cancer Letter, Nov. 6, 2009).

A court document showing an Amgen spreadsheet lays out the financial gains that doctors were encouraged to capitalize on, via the overfilled prescriptions.

Amgen "conspired to encourage medical providers to purchase Aranesp based on representations of the profits that the providers could realize from submission of inflated Aranesp-related claims to Medicare," and "encouraged medical providers to overstate the amount of Aranesp administered so that the provider could achieve greater amounts of reimbursement form Medicare and/or Medicaid, thereby making Aranesp more attractive than competitive drugs," the lawsuit stated.

## NCI-MATCH Trial Opens

ECOG-ACRIN opened the NCI-MATCH precision medicine trial, the largest, most scientifically rigorous precision medicine trial in cancer to date.

NCI-MATCH seeks to determine whether matching certain drugs or drug combinations to people whose tumors have specific gene abnormalities will effectively treat their cancer, regardless of their cancer type.

Known to doctors as the phase II trial EAY131, the treatment focuses on molecular abnormalities of patient tumors instead of the organ sites of the cancer.

NCI-MATCH will match patients with one of 22 treatments to test the use of each specific drug or drug combination targeted to a particular gene abnormality. It is open to medical facilities with 10 treatments, and the additional 12 treatments will be added to the trial within the next several months.

Patients can enroll in the trial on a rolling basis as hospitals and cancer centers join and as the additional treatments become available.

The trial seeks to enroll for genetic testing about 3,000 adults, 18 years of age and older, with any type of solid tumor or lymphoma that has returned or gotten worse after standard systemic therapy. Patients may also be eligible for screening if they have a rare type of cancer for which there is no standard treatment.

All patients considering the trial will need to have a new biopsy and their tumor cells will need to undergo genetic testing to see whether they contain one of the gene mutations being studied.

Trial researchers expect that about one-third of the patients screened will have one or more molecular abnormalities that match one of the 22 treatments being studied. If so, they will be further evaluated to determine if they are able to be treated as part of the trial.

There will be 35 patients enrolled for each drug/drug combination being studied. The trial's design calls for at least 25 percent of the 1,000-patient enrollment to be people with rare types of cancer.

ECOG-ACRIN is coordinating the genetic testing. It also supports all trial sites with training, laboratory services, trial assignments, biostatistical support, data management, auditing, quality control, and public awareness. The study was co-developed by the ECOG-ACRIN Cancer Research Group and NCI.

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# ASCO Updates Policy on Genetics and Genomic Testing

The American Society of Clinical Oncology issued an updated policy statement on genetic and genomic testing for cancer susceptibility.

Published in the Journal of Clinical Oncology, the statement reviews the ways in which new technologies are transforming the assessment and identification of inherited cancer susceptibility, and makes a series of recommendations for the optimal deployment of these technologies in oncology practice.

"As cancer diagnosis and treatment is becoming more genetically-driven, new opportunities and questions are emerging about screening for hereditary cancers," said ASCO President Julie Vose. "ASCO is releasing this updated policy statement at this critical juncture to ensure that all interested parties thoughtfully consider these concerns as the future of genetic and genomic testing for cancer susceptibility unfolds."

Mark Robson, chair of ASCO's Ethics Committee and lead author of the ASCO policy statement, said: "As this promising field moves forward, we must ensure that providers are well versed in the diagnostic and treatment options available, that patients have access to genetic testing that identifies hereditary risk, and that these tests have appropriate regulatory oversight."

The policy statement, titled "Genetic and Genomic Testing for Cancer Susceptibility," reviews and makes recommendations in the following five key areas:

**Germ-line Implications of Somatic Mutation Profiling**

ASCO calls for further research to develop best practices for the delivery of incidental and secondary germ-line findings. The society also encourages research aimed at improving understanding of patient preferences, optimal pre-test education and informed consent, and multilevel outcomes (i.e., patient, provider, health care system delivery, and cost) in this area. Further, ASCO recommends that laboratories choosing to conduct secondary analyses should develop mechanisms to report only somatic results for patients who decline to receive germ-line findings.

**Multi-gene Panel Testing for Cancer Susceptibility**

Providers with particular expertise in cancer risk assessment should be involved in ordering and interpreting multi-gene panels that include genes of uncertain clinical utility and genes not suggested by the patient's personal and/or family history. Further, ASCO encourages research to delineate the optimal use of panel-based testing, development of evidence-based practice guidelines as data emerges, and education of providers on the challenges of using these tests.

**Quality Assurance in Genetic Testing**

ASCO recommends appropriate regulation of tests that detect inherited genetic variants and supports a risk-based approach to FDA regulation for laboratory-developed tests and commercial tests--in a manner that does not compromise innovation or limit patient access to testing. High-quality standards should be adopted that allow providers and patients to understand the accuracy, benefits, and limitations of genetic tests conducted by individual laboratories.

**Education for Oncology Professionals**

ASCO recommends continued education of oncologists and other healthcare professionals in cancer risk assessment and the management of individuals with inherited predisposition to cancer. Further, ASCO recommends that oncology training programs develop a set of core skills for new trainees and ensure adequate time for achieving these skills.

**Access to Cancer Genetics Services**

ASCO calls for coverage policies that support access to cancer risk assessment and prevention services for individuals who are suspected to be at increased genetic risk. Further, ASCO opposes any payment policies that have the potential to negatively impact the care of cancer patients by serving as a barrier to the appropriate use of genetic testing services.

*Obituary*

# UNMC's Sidney Mirvish, 86

Cancer researcher Sidney Mirvish died at age 86. His research into nitrosamines and carcinogenesis led to changes in the way lunch meats, hot dogs and sausages were made.

Mirvish served as professor emeritus in the Eppley Institute for Research in Cancer and Allied Diseases at the University of Nebraska Medical Center, where he was faculty member for 46 years. Mirvish died due to complications following emergency surgery on Aug. 18.

Ken Cowan, director of the Fred & Pamela Buffett Cancer Center, called him "an internationally recognized leader in nitrosamines and carcinogenesis who helped build the scientific reputation of UNMC and the Eppley Institute."

"Sidney was a remarkable individual and scientist," Cowan said. "His continued passion for science and the Eppley Institute was truly inspirational."

Samuel Cohen, Havlik-Wall Professor of Oncology, Pathology and Microbiology, knew Mirvish for 45 years, first at Wisconsin, then at UNMC. "He was an outstanding scientist, known for his seminal research on carcinogenic N-nitrosamines," Cohen said. "He was the first to show their formation from nitrites in food, and the inhibition of this formation by vitamin C."

"Despite severe visual impairment, he was a highly productive scientist, with NCI support continuing into his 80s," Cohen said. "He was not only a renowned scientist, but was an avid collector of South African art and artifacts, and was a generous, friendly, warm human being, friend and colleague. He will be greatly missed."

Mirvish completed his doctorate degree in organic chemistry at Cambridge University in England and received his bachelor's and master's degrees at the University of Cape Town in South Africa. After working in South Africa at the University of Witwatersrand, he joined the Weizmann Institute in Israel where he developed his interest in carcinogenesis.

After working briefly at the McArdle Laboratory for Cancer Research at the University of Wisconsin, he was recruited as an associate professor to the Eppley Institute in 1969. He was promoted to professor in 1977, served as interim director and associate director of the institute from 1981-1986, and received the Outstanding Research and Creativity Award from the University of Nebraska in 1986.

Mirvish authored 155 publications and his lab was funded by the NCI through 2013, as professor emeritus. He was still working on grant applications and research manuscripts and continued to come regularly to institute seminars and meetings.

UNMC Chancellor Emeritus Harold Maurer called Mirvish "a quiet, unassuming man," despite his accomplishments as a scientist. "In the summer, you would see him walking to work in shorts and wearing a backpack," Maurer said. "He exhibited the essence of diversity at UNMC. It gave UNMC character! I'll miss him."

Mirvish is survived by his wife, Lynda; two children, Leora Mirvish and Daniel Mirvish, his wife, Rachel, and their three children, Rebecca, Jonathan and Miriam. He also is survived by his sister, Doreen Bahiri.

"Dr. Mirvish was a gentle soul. His kindness, thoughtful compassion and dedication to research and teaching was at the highest level. As a teacher he taught by example and as friend he lived by example. He also cared more about others than himself and was always the first in the lecture hall, the conference room and the one asking the most provocative questions about science, truth and life. He was the next generation that has aged and perhaps moved on. I will miss his wisdom dearly. Most importantly I will miss him as a man who influenced our commitment to Nebraska, the medical center and to God."

- Howard Gendelman, Margaret R. Larson Professor of Internal Medicine and Infectious Diseases; chair, UNMC Department of Pharmacology and Experimental Neuroscience

"If you wanted to point to someone who loved his work, Sidney would have been a great choice. Even as an emeritus professor, he was working. In fact, he was on the list for a March 2016 NIH grant submission. We would all be blessed to have the enduring passion for our profession that Sidney had for his."

- Robert Lewis, professor, Eppley Institute for Research in Cancer and Allied Diseases; program leader, Fred & Pamela Buffett Cancer Center

"While I never worked directly with him, I had the pleasure of discussing science and various other lighter topics numerous times with Sidney. What a great person and what exemplary dedication to science. He will be missed."

- Howard Fox, senior associate dean of research and development, UNMC College of Medicine;

professor and executive vice chair, UNMC Department of Pharmacology and Experimental Neuroscience

"Sidney Mirvish was a scientist through and through. Long after he officially retired, he continued to discuss his ideas and write grants. He also continued to go to seminars. If the speaker skipped over some background information or used some unfamiliar jargon, Sidney was sure to ask for clarification. It would often take the speaker by surprise, but not most in the audience. We had seen it all many times over the years. Sometimes, Sidney's questions were the most insightful ones asked because his questions would get to the heart of the issue. He will be missed."

- Angie Rizzino, professor, Eppley Institute for Research in Cancer and Allied Diseases

"We think everybody on campus recognized Sidney. Because of vision challenges he would always sit in the front row at seminars and scrutinize your slides in great detail. It was rather intimidating, since you though he might be picking out all the errors. In fact he would skip the small stuff and ask important and insightful questions. He was especially helpful to the Lymphoma Research Group because he was so very knowledgeable as an advisor and collaborator on studies of exposure to agricultural chemicals implicated in causing cancers."

- Graham Sharp, and Shantaram Joshi, professors, UNMC Department of Genetics, Cell Biology & Anatomy

"I did not know Sidney well and had little interaction with him. He did come to our departmental seminars for many years and the thing that impressed me about him was that he was not afraid to ask a question about any subject. This is a valuable characteristic and something we try (frequently unsuccessfully) to instill in our students. If you do not ask questions, you will not learn much."

- Charlie Murrin, retired professor, pharmacology and experimental neuroscience



*In Brief*

## Edith Mitchell Named President Of the National Medical Association

(Continued from page 1)

"I am deeply honored to have been appointed as president-elect of this prestigious organization," said Mitchell Aug. 3, who is also the program leader of Gastrointestinal Oncology and associate director for diversity programs at Thomas Jefferson University.

"There is still much work to be done with regards to disparities in medical treatment. I believe that we can all work together and make great strides to address barriers in helping underserved populations get better care and lead to better health care in our nation."

The NMA is the nation's oldest and largest professional society for African American physicians. One of its mission statements is to support and increase the representation and contributions of people of African descent by helping shape policy, through educational programs, and community outreach.

Mitchell's work has focused on groups whose medical needs have not been met by medical system in the United States. As a practicing medical oncologist, her research interests have included many cancer types such as breast, colorectal, pancreatic and other gastrointestinal malignancies.

In 2008, she received the Tree of Life award from the Wellness of You organization, a Philadelphia nonprofit providing health education and resources to the community, in recognition of her efforts in health management in the local and global community.

She was recognized for her commitment to diversity, research, and education in 2009 by the American Cancer Society's Cancer Control Award.

Mitchell is also a retired brigadier general in the U.S. Air Force, and was the first female physician to attain this rank. She served as senior medical Air National Guard advisor to the command surgeon and was the medical liaison between the active Air Force and the Air National Guard.

**ROBERT DIPAOLA, STEPHEN GRUBER** and **CANDACE JOHNSON** were elected to the board of directors of the **Association of American Cancer Institutes**. Their three-year terms will begin Oct. 25, during the annual meeting of the AACI and the Cancer Center Administrators Forum in Washington, D.C.

DiPaola is director of the Rutgers Cancer Institute of New Jersey. He has held multiple local and national positions including the founding director and program

leader of the Prostate Cancer Center at the Cancer Institute of New Jersey; national chairman of the Genitourinary Committee of the Eastern Oncology Cooperative Group; chief of Medical Oncology at Robert Wood Johnson Medical School; and was appointed as director of the CINJ in 2008.

Gruber was appointed director of the USC Norris Comprehensive Cancer Center in 2011. He is a professor of medicine and preventive medicine, and holds the H. Leslie and Elaine S. Hoffman Cancer Research Chair at the University of Southern California. Prior to his appointment at USC Norris, Gruber was associate director of cancer prevention and control at the University of Michigan Comprehensive Cancer Center.

As president and chief executive officer of Roswell Park Cancer Institute, Johnson oversees all cancer research, patient care, and NCI core funding. Johnson also serves as the Wallace Family Chair in Translational Research and as a professor of oncology. Prior to her appointment, Johnson was deputy director of the institute and also chair of the Department of Pharmacology and Therapeutics for more than a decade.

**FRANCIS COLLINS**, director of the NIH, was awarded the Leadership in Personalized Medicine Award by the **Personalized Medicine Coalition**. He will be presented the award during the Personalized Medicine Conference at Harvard Medical School Nov. 19.

In his letter nominating Collins for the award, Harvard Medical School professor Raju Kucherlapati, noted that Collins "has made sustained and critical contributions for the establishment of personalized medicine."

Collins earned national recognition in 1989, more than a decade before the complete sequencing of the human genome, for his team's discovery of the gene responsible for cystic fibrosis. He then served as the director of the National Human Genome Research Institute, where he was the overall project manager of the international Human Genome Project, which produced a complete map of the human genome in 2003.

He also played a key role in the passage of the Genetic Information Nondiscrimination Act in 2008, which has helped to ensure that the insights from his extraordinary achievements and those of many others are not used for discriminatory purposes.

President Barack Obama nominated him as NIH director in 2009, proclaiming that his work had already "changed the very ways we consider our health and examine disease." As director, Collins' advocacy helped shape the Precision Medicine Initiative, which was announced earlier this year as part of the president's budget proposal for fiscal year 2016.

"I see a day in the not too distant future when every person will have his or her genome sequenced and other important data collected as a routine part of medical care with individualized strategies developed for diagnosing, treating and preventing their disease," said Collins. "I know that the PMC shares this vision and I am truly honored to receive this award from an organization that continues to pursue the vision with such great passion."

**MASSIMO CRISTOFANILLI** was appointed associate director for precision medicine and translational research at the **Robert H. Lurie Comprehensive Cancer Center of Northwestern University** and director of Northwestern OncoSET.

Cristofanilli will serve as a professor of medicine in the Division of Hematology-Oncology at Northwestern University Feinberg School of Medicine. His work has focused on the translational research and treatment of patients with inflammatory breast cancer.

Cristofanilli comes to Northwestern from Thomas Jefferson University, where he served as director of Jefferson Breast Care Center and deputy director of Translational Research at the Kimmel Cancer Center.

Previously, Cristofanilli was chair of the Department of Medical Oncology at Fox Chase Cancer Center, and executive director of the Morgan Welch Inflammatory Breast Cancer Program and Clinic at MD Anderson Cancer Center.

As associate director for precision medicine and director of Northwestern OncoSET, Cristofanilli will oversee the development of OncoSET and related clinical and research operations. The program involves sequencing tumor genetic profiles and evaluating the results to provide the treatments or clinical trials that will offer the greatest benefit.

**JEFFREY RATHMELL** and **W. KIMRYN RATHMELL** were both appointed to leadership roles at **Vanderbilt University Medical Center**.

W. Kimryn Rathmell was named director of Vanderbilt University Medical Center's Division of Hematology and Oncology, and her husband, Jeffrey, will lead a new Vanderbilt Center of Immunobiology.

Previously, W. Kimryn Rathmell was the Alexander Professor for Translational Science and associate director for Training and Education at

University of North Carolina Chapel Hill Lineberger Comprehensive Cancer Center. Her research focuses on the genetic and molecular signals that drive renal cell carcinomas and specializes in the treatment of patients with rare kidney cancers, as well as prostate, bladder and testicular cancer.

At UNC, she also served as a director for the Medical Scientist Training Program and led the mentoring activities of the Hematology and Oncology Division and the Lineberger Cancer Center.

In her current research, Rathmell and colleagues have identified factors that are critical to transitions in the progression of kidney cancer. She has also led or participated in a number of the Cancer Genome Atlas projects.

Rathmell has received the American Society of Clinical Oncology Leadership Development Award, the American Association for Cancer Research Landon INNOVATOR Award for Personalized Medicine, the Ruth and Philip Hettleman Award for Scholarly Achievement, the Doris Duke Clinical Translational Scientist Award, and the V Scholar Award from the V Foundation for Cancer Research.

Jeffrey Rathmell was named a professor of Pathology, Microbiology and Immunology at Vanderbilt, and will also serve as co-leader of the Host Tumor Interactions Research Program. The Center for Immunobiology is supported by the Department of Pathology, Microbiology and Immunology, the Department of Medicine, and Vanderbilt-Ingram Cancer Center.

Rathmell comes to Vanderbilt from Duke University Medical Center, where he served as associate professor of Pharmacology and Cancer Biology and of Immunology in the Duke Molecular Physiology Institute, as well as director of Graduate Studies of Pharmacology.

In his laboratory research, Rathmell has examined the metabolism of blood cells. His work at Vanderbilt will focus on the field of immunometabolism and how nutrient and metabolic pathways can influence immune responses in normal and diseased settings.

He received the Sidney Kimmel Foundation for Cancer Research Scholar Award from the National Cancer Institute, the Scholar Award from the V Foundation for Cancer Research, was named a Research Scholar by the American Cancer Society, the Bernard Osher Fellow of the American Asthma Society and a Leukemia and Lymphoma Scholar.

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**LOIS TRAVIS** was named the Lawrence H. Einhorn Professor of Cancer Research at the Indiana University School of Medicine and director of the Cancer Survivorship Research Program at the **IU Melvin and Bren Simon Cancer Center**.

Travis is also a member of the cancer center's Cancer Prevention and Control research program, which focuses on prevention, early detection and survivorship, and she will also hold an academic appointment in the Department of Epidemiology at the IU Richard M. Fairbanks School of Public Health.

In addition, Travis is the principal investigator of an NIH study that aims to identify genetic variants associated with cisplatin-related toxicities, and focuses on testicular cancer patients previously treated at the IU Simon Cancer Center and other major cancer centers.

Previously, Travis was the director of the Rubin Center for Cancer Survivorship and chief of the Division of Cancer Survivorship at the University of Rochester Medical Center. She also was a senior principal investigator and lead research investigator at the NCI, where for nearly 20 years she conducted international studies of late treatment effects in cancer survivors, with an emphasis on second malignant neoplasms.

**RACHEL HUMPHREY** was named chief medical officer of **CytomX**. Humphrey previously served as a member of the company's board of directors.

Humphrey formerly led immuno-oncology at Eli Lilly and AstraZeneca, and also oversaw clinical development of Yervoy (ipilmumab) at Bristol-Myers Squibb and the development of Nexavar (sorafenib) at Bayer.

Humphrey recently held positions as vice president and head of immuno-oncology at Eli Lilly and at AstraZeneca, where she was responsible for building the immuno-oncology departments and supervising the strategies and designs for all the immuno-oncology agents in development.

She previously served as vice president of product development at Bristol-Myers Squibb, where she led all aspects of the clinical development of Yervoy through the submission of global biologics license applications and global launch.

At Bayer, Humphrey supervised the early and late stage clinical development of Nexavar for treatment of renal cell carcinoma. She began her career as an oncology fellow and staff physician at the NCI.

In connection with her appointment as chief medical officer, Humphrey will resign from the board of directors of CytomX.

**DONALD SHELDON** was appointed to the new role of regional president of community hospitals for **University Hospitals.**

Sheldon has served as president of UH Elyria Medical Center since 2009, and prior to that served for 10 years as Elyria's chief medical officer.

Sheldon has many years of experience as an emergency physician and was medical director of his emergency medicine group and department. He serves on many community groups' boards, including the Lorain County Free Clinic, for which he has served as a volunteer physician, medical director and board member since its inception in 1986.

**KEITH PERRY** was named as chief information officer of **St. Jude Children's Research Hospital.**

Perry joins St. Jude from MD Anderson Cancer Center where he served as associate vice president and deputy chief information officer.

He helped manage the division's 290 million dollar annual budget, and implemented high performance computing programs to support research and clinical applications, such as next-generation genomic sequencing and proton beam modeling.

**NORTHWESTERN MEDICINE** and the Robert H. Lurie Comprehensive Cancer Center of Northwestern University officially named the **Lynn Sage Cancer Research Foundation Breast Cancer OncoSET program.**

LSCRF Breast Cancer OncoSET will combine oncology with genomic tumor profiling. The program will initially focus on patients with breast cancer that is non-responsive to traditional therapeutic treatments, and will serve as an extension of the Northwestern OncoSET program that was first launched earlier this year by the Lurie Cancer Center, in collaboration with Northwestern Memorial Hospital.

The Breast Cancer OncoSET program was made possible by a generous donation from the Lynn Sage Cancer Research Foundation, which is the first major naming gift that a Northwestern OncoSET program has received.

**THE CANCER PREVENTION AND RESEARCH INSTITUTE OF TEXAS** awarded seven grants through its academic research program. The grants, totaling $23 million, support the recruitment of seven cancer scientists to academic institutions in Texas, including two distinguished senior researchers.

*The awarded grants include the recruitment of first-time, tenure-track faculty members:*

**Charles Lin**, recruitment to Baylor College of Medicine from the Dana-Farber Cancer Institute – $2,000,000

**Leng Han**, recruitment to The University of Texas Health Science Center at Houston from MD Anderson Cancer Center – $2,000,000

**Jan Erzberger**, recruitment to The University of Texas Southwestern Medical Center from ETH Zurich (Eidgenossische Technische Hochschule) – $2,000,000

**Kendra Frederick**, recruitment to The University of Texas Southwestern Medical Center from the Whitehead Institute for Biomedical Research – $3,000,000

**Peter Douglas**, recruitment to The University of Texas Southwestern Medical Center from the University of California, Berkeley – $2,000,000

*The awards also include the recruitment of established investigators:*

**Frank McKeon**, recruitment to the University of Houston from the Genome Institute of Singapore – $6,000,000

**Yang-Xin Fu**, recruitment to The University of Texas Southwestern Medical Center from the University of Chicago – $6,000,000

Additionally, members of the CPRIT Oversight Committee elected **Pete Geren** as presiding officer and **Will Montgomery** as vice presiding officer. Geren, who was vice presiding officer, replaces **William Rice**, whose term as presiding officer expired. **Amy Mitchell** was re-elected as secretary of the committee. Geren, Montgomery and Mitchell have been on the commitee since 2013.

Geren is the president of the Sid W. Richardson Foundation. From 2001 to 2009, he served in the U.S. Department of Defense as special assistant to the secretary of defense, acting secretary of the Air Force, undersecretary of the Army and secretary of the Army. He also served four terms in the House of Representatives and was formerly an assistant to Sen. Lloyd Bentsen.

Montgomery is a partner at the law firm Jackson Walker LLP, where his practice focuses on commercial litigation and arbitration.

Mitchell, a cancer survivor, works as an attorney in the real estate practice group of Fulbright & Jaworski's Austin office. She has been included in Real Estate Law's "The Best Lawyers in America" listing for the past six years and was named "Texas Top Rated Lawyer" by LexisNexis Martindale-Hubbell.

*Drugs and Targets*

# FDA Approves Varubi For Nausea and Vomiting

**FDA approved Varubi (rolapitant)** to prevent delayed phase chemotherapy-induced nausea and vomiting.

Varubi, marketed by Tesaro Inc., is approved in adults in combination with other antiemetic agents that prevent nausea and vomiting associated with initial and repeat courses of vomit-inducing cancer chemotherapy.

Nausea and vomiting that occurs from 24 hours to up to 120 hours after the start of chemotherapy is referred to as delayed phase nausea and vomiting. Prolonged nausea and vomiting can lead to weight loss, dehydration and malnutrition in cancer patients leading to hospitalization.

Varubi is a substance P/neurokinin-1 receptor antagonist. Activation of NK-1 receptors plays a central role in nausea and vomiting induced by certain cancer chemotherapies, particularly in the delayed phase. Varubi is provided to patients in tablet form.

The safety and efficacy of Varubi were established in three randomized, double-blind, controlled clinical trials where Varubi in combination with granisetron and dexamethasone was compared with a control therapy (placebo, granisetron and dexamethasone) in 2,800 patients receiving a chemotherapy regimen that included highly emetogenic (such as cisplatin and the combination of anthracycline and cyclophosphamide) and moderately emetogenic chemotherapy drugs. Those patients treated with Varubi had a greater reduction in vomiting and use of rescue medication for nausea and vomiting during the delayed phase compared to those receiving the control therapy.

Varubi inhibits the CYP2D6 enzyme, which is responsible for metabolizing certain drugs. Varubi is contraindicated with the use of thioridazine, a drug metabolized by the CYP2D6 enzyme, because use of the two drugs together may increase the amount of thioridazine in the blood and cause an abnormal heart rhythm. The most common side effects in patients treated with Varubi include a low white blood cell count (neutropenia), hiccups, decreased appetite and dizziness.

**The European Commission granted a marketing authorization for Unituxin (dinutuximab)** for the treatment of high-risk neuroblastoma in patients aged 12 months to 17 years, who have previously received induction chemotherapy and achieved at least a partial response, followed by myeloablative therapy and autologous stem cell transplantation.

Unituxin is administered in combination with granulocyte-macrophage colony-stimulating factor, interleukin-2, and isotretinoin.

The European approval was based on demonstration of improved event-free survival and overall survival in a multicenter, open-label, randomized trial (ANBL0032) sponsored by NCI under a Cooperative Research and Development Agreement with the drug's sponsor, United Therapeutics Corp., and conducted by the Children's Oncology Group.

The trial randomized (1:1) 226 patients to either the Unituxin/13-cis-retinoic acid arm or to RA alone. Patients in each arm received six cycles of treatment.

The Unituxin/RA arm consisted of Unituxin in combination with GM-CSF and RA (cycles 1, 3, and 5), Unituxin in combination with IL-2 and RA (cycles 2 and 4), and RA (cycle 6). Patients were 11 months to 15 years of age, with a median age 3.8 years.

The major efficacy outcome measure was investigator-assessed EFS, defined as the time from randomization to the first occurrence of relapse, progressive disease, secondary malignancy or death.

The primary intent-to-treat analysis found an improvement in EFS associated with Unituxin immunotherapy plus isotretinoin as compared to isotretinoin alone. The two-year estimates of EFS were 66 percent among subjects receiving Unituxin immunotherapy plus isotretinoin as compared with 48 percent in subjects receiving isotretinoin alone (log-rank test $p = 0.033$), although this difference did not reach formal statistical significance according to the pre-specified plan for interim analyses.

In addition, OS was evaluated with three years of follow-up after the EFS analysis as a secondary endpoint with a significant improvement observed among ITT subjects randomly allocated to receive Unituxin immunotherapy plus isotretinoin as compared with isotretinoin alone. The three-year estimates of OS were 80 percent compared with 67 percent among subjects receiving Unituxin immunotherapy plus isotretinoin and isotretinoin alone, respectively (log-rank test $p = 0.0165$).

Long-term overall survival was evaluated with five years of follow up after the EFS analysis and continued to demonstrate a survival advantage for patients who received Unituxin immunotherapy compared to those who received isotretinoin alone. The five-year estimates of OS were 74 percent for Unituxin immunotherapy compared to 57 percent for isotretinoin alone (log-rank test $p = 0.030$).

The most frequently occurring adverse reactions

reported during the neuroblastoma studies were hypotension, pain, hypersensitivity, pyrexia, urticaria, capillary leak syndrome, anemia, hypokalemia, decreased platelet count, hyponatremia, increased alanine aminotransferase, decreased lymphocyte count and decreased neutrophil count. Additional adverse reactions characteristic of an allergic response were also reported, including anaphylactic reaction and bronchospasm.

Unituxin is a monoclonal chimeric antibody composed of murine variable heavy and light chain regions and the human constant region for the heavy chain kappa, and reacts specifically with the ganglioside GD2, which is highly expressed on the surface of the neuroblastoma cells and minimally expressed on the surface of normal human neurons, peripheral pain fibres, and skin melanocytes.

In March, Unituxin, in combination with GM-CSF, IL-2 and RA, became the first therapy to be approved by FDA for the treatment of pediatric patients with high-risk neuroblastoma who achieve at least a partial response to prior first-line multi-agent multimodality therapy.

Unituxin carries a Boxed Warning alerting patients and health care professionals that Unituxin irritates nerve cells, causing severe pain that requires treatment with intravenous narcotics and can also cause nerve damage and life-threatening infusion reactions, including upper airway swelling, difficulty breathing, and low blood pressure, during or shortly following completion of the infusion. Unituxin may also cause other serious side effects including infections, eye problems, electrolyte abnormalities and bone marrow suppression.

**FDA granted Orphan Drug Designation to Toca 511 & Toca FC**, an investigational immunotherapy treatment for glioblastoma developed by Tocagen.

The agency recently granted the drug Fast Track designation for the treatment of recurrent high-grade glioma, which includes glioblastoma and anaplastic astrocytoma. According to Tocagen, the drug is planned to move into a clinical trial later this year.

Toca 511 & Toca FC is an investigational treatment that is designed to program cancer cells to convert the prodrug 5-FC into the anticancer drug 5-FU, killing tumor cells and leading to activation of the immune system via a combination of mechanisms.

Toca 511 is a retroviral replicating vector that selectively delivers a gene for the enzyme cytosine deaminase to the tumor. Patients then take oral cycles of Toca FC, a novel formulation of an antifungal drug, which is converted within infected cancer cells into the FDA-approved anticancer drug, 5-fluorouracil. Immune activation locally in the tumor occurs through a combination of mechanisms that together break the barrier of immune tolerance and may lead to durable tumor response, according to Tocagen.

**FDA granted Orphan Drug Designation for MTG-201**, a therapy targeting Dickkopf-3 gene defects in various cancers, for the treatment of malignant mesothelioma.

The Dickkopf-3 gene produces a protein called REIC (Reduced Expression in Immortalized Cells protein), which is a critical protein in the downstream mechanism of apoptosis and when absent cancer cells cannot die.

By expressing REIC protein from within cancer cells, MTG-201 induces selective apoptosis due to ER stress, directly killing the cancer and reducing cancer burden. MTG-201 also stimulates the production of activated T-cell lymphocytes that specifically target and destroy residual cancer cells.

MTG-201, developed by MTG Biotherapeutics, is currently in phase I clinical trials for the treatment of prostate cancer and mesothelioma. Preclinical programs are ongoing for the treatment of liver and bladder cancers. MTG-201 is also being evaluated for efficacy in combination with anti-PD-1, anti-PD-L1 and anti-CTLA-4 antibodies.

**FDA granted priority review for MCNA**, developed by Telesta Therapeutics Inc.

The FDA completed its initial review of Telesta's biologics license application and accepted it for filing. The agency set Feb. 27, 2016 as the review goal date for MCNA. The FDA has also advised that it will be organizing an advisory committee to discuss the BLA application.

MCNA is a biologic therapy developed to treat high-risk, non-muscle invasive bladder cancer patients who are refractory to or relapsing from front-line therapy, and is derived from the cell wall fractionation of a non-pathogenic bacteria. Its activity is believed to be through a dual mechanism of immune stimulation and direct anti-cancer effects.

MCNA was developed to be delivered as a sterile suspension for intravesical administration by urologists and urology nurses, following the same dosing paradigm as first-line bacillus Calmette-Guérin therapy. The efficacy, duration of responses and safety data from MCNA's phase III trial was recently published in The Journal of Urology.