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Thumbs Up on Amgen's T-VEC to Treat Melanoma; Is it Local Therapy for Systemic Disease?

By Paul Goldberg

An FDA advisory committee April 29 recommended approval of a metastatic melanoma treatment based on an attenuated Herpes Simplex Virus-1.

In a joint meeting, the agency's Oncologic Drugs Advisory Committee and its Cellular, Tissue, and Gene Therapies Advisory Committee voted 22 to 1 to recommend full approval for talimogene laherparepvec, sponsored by Amgen Inc.

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NIH Slated to Receive $10 Billion Increase In Second 21st Century Cures Draft Bill

By Matthew Bin Han Ong

The House Committee on Energy and Commerce published the second "discussion draft" for a comprehensive bipartisan initiative aimed at streamlining development of drugs and medical devices.

The proposed legislation, called "21st Century Cures," was launched April 30, 2014, and is led by Rep. Fred Upton (R-Mich.), chairman of the committee, and Rep. Diana DeGette (D-Colo.), chief deputy whip.

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In Brief

Kripke to Step Down as CPRIT Chief Scientist

MARGARET KRIPKE is leaving her position as chief scientific officer at the **Cancer Prevention and Research Institute of Texas**.

In a statement, Kripke said she had met her goals at the institute:

"I came to CPRIT nearly two-and-a-half years ago to see if I could help reconstitute the research peer review committees and restart the research grants program," she wrote.

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CBER Staff Resisted Requests to Rephrase Approval Question

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At the contentious all-day meeting, which ran twice as long as a standard session of ODAC, the unusually large group of advisors summoned by the FDA didn't get the opportunity to clearly identify the group of patients who stand to benefit from the agent, also called T-VEC, or specify the agent's place in a sequence of melanoma treatments.

One panel member—NCI surgeon Richard Sherry—pressed to narrow the indication, which, according to data, is active in cutaneous lesions and less active (or inactive) in visceral disease.

"Does it further the discussion or weaken the discussion not to step up to the plate and define whom this makes sense in?" Sherry said. "You can't just leave it open."

In explanation of their votes on the single approval question, several committee members said they would have been more comfortable had the questions been broken down into several question, to give them the option to limit the population of patients who may be candidates for this therapy.

Nonetheless, the agency pressed for an up-or-down vote on a single question.

Visibly disappointed by his failure to convince the agency to reframe this approval question, Sherry said repeatedly that unrestricted use of what may or may not be a local therapy for a systemic disease has the potential to harm patients. He ended up casting the sole dissenting vote, and in the end the sponsor secured the advisory committee's endorsement for a broad indication.

Despite having seized the day, Amgen issued a restrained statement at the conclusion of the meeting.

"It is clear from today's discussion that the committee recognized the importance of the need for new therapeutic options for patients with metastatic melanoma," the company said. "We look forward to talking with the FDA about how to best make talimogene laherparepvec monotherapy available to patients as they complete their review of the Biologics License Application."

The reason for PR restraint may have to do with the history of what happens when cellular, tissue and gene therapies for cancer go through FDA approval. The T-VEC application went through the agency's Center for Biologics Evaluation and Research, which has a smaller oncology staff than the Center for Drug Evaluation and Research.

Eight years ago, the Oncologic Drugs Advisory Committee and the Cellular, Tissue, and Gene Therapies Advisory Committee famously met to consider the Dendreon Inc. cellular therapy Provenge (sipuleucel-T), giving it overwhelming thumbs-up, but the agent wasn't immediately approved as FDA asked for new studies (The Cancer Letter, April 13, 2007). Provenge was ultimately backed with data and approved.

The committee discussion of T-VEC differed from its discussion of Provenge. At the Provenge meeting, oncology experts were in a small minority. At the T-VEC meeting, people who understand cancer in general and melanoma in particular were present and vocal.

Sherry was heard clearly and repeatedly, and many of those who voted for approval made comments that indicated that they clearly understood the limitations of the data presented by Amgen and potential pitfalls of a broad indication.

FDA's undisputed cancer czar Richard Pazdur, director of the Office of Hematology and Oncology Products in CDER, was present at the Provenge meeting. His absence at the T-VEC meeting was difficult to miss. He was neither at the committee table nor in the audience.

While the rationale for Pazdur's absence isn't publicly known, loss of authority should be eliminated from the list of possible explanations. If anything, Pazdur's influence at the agency has grown. Earlier this year, he played a role in speeding up approval of a lung cancer therapy (The Cancer Letter, March 6, 2015).

There is no question that FDA staff understood the regulatory issues involved in the T-VEC application. The briefing documents reflect the following concerns:

Cover Photo: NCI's Richard Sherry, who tried unsuccessfully to refocus FDA's approval question.

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Source: ODAC briefing documents

FDA-Approved Products	Approval Year/ indication	Endpoint(s)	Clinical Benefit / Effect
DTIC (dacarbazine)	**1975**	**ORR**	**ORR of 5-20%**
Proleukin (Interleukin-2)	**1998**	**ORR (WHO)**	**ORR 16% (CR 6%); CR: 59+ (range 3 to 122+ months) PR or CR: 59 months+ (range 1-122+ months)**
Yervoy (Ipilimumab)	**March 25, 2011 treatment of unresectable or metastatic melanoma**	**OS ORR (WHO)**	**Ipi vs. gp100: OS: HR 0.66 (95% CI: 0.51, 0.87) median 10 vs. 6 months BORR: 10.9% vs. 1.5%** **Ipi+gp100 vs. gp100: OS: HR 0.68 (95% CI: 0.55, 0.85) median 10 vs. 6 months BORR: 5.7% vs. 1.5%**
Patients with unresectable or metastatic melanoma and BRAF V600E mutations			
Zelboraf (Vemurafenib)	**2011**	**OS PFS**	**Vemurafenib vs. DTIC mOS: 13.6 vs. 10.3 months HR: 0.44 (95% CI: 0.33, 0.59)** **mPFS: 5.3 vs. 1.6 months HR: 0.26 (95% CI: 0.20, 0.33)**
Tafinlar (Dabrafenib)	**2013**	**PFS**	**Dabrafenib vs. Dacarbazine mPFS: 5.1 vs. 2.7 months HR: 0.33 (95% CI: 0.20, 0.54)**
Mekinist (Trametinib)	**2013**	**PFS**	**Trametinib vs. Chemotherapy mPFS: 4.8 vs. 1.5 months HR: 0.47 (95% CI: 0.34, 0.65)**
Tafinlar and Mekinist (Dabrafenib and Trametinib)	**2014 Accelerated Approval**	**ORR***	**Dabrafenib plus or minus Trametinib ORR 76% vs. 54% mDOR : 10.5 months (95% CI : 7, 15) vs 5.6 months (95% CI : 5, 7)**
Patients with unresectable or metastatic melanoma with disease progression following ipilimumab and/or BRAF inhibitor			
Keytruda (Pembrolizumab)	**2014 Accelerated Approval**	**ORR***	**24% (95% CI: 15, 34) CR(1) PR (20), 86% ongoing response (1.4 – 8.5 months)**
Opdivo (Nivolumab)	**2014 Accelerated Approval**	**ORR***	**32% (95% CI: 23, 41) CR(4) PR (34)**

• Appropriateness of the study control;

• Differential outcome assessments in the two arms of the study;

• Reliability of response assessments;

• Meaningfulness of the primary endpoint of durable response rate;

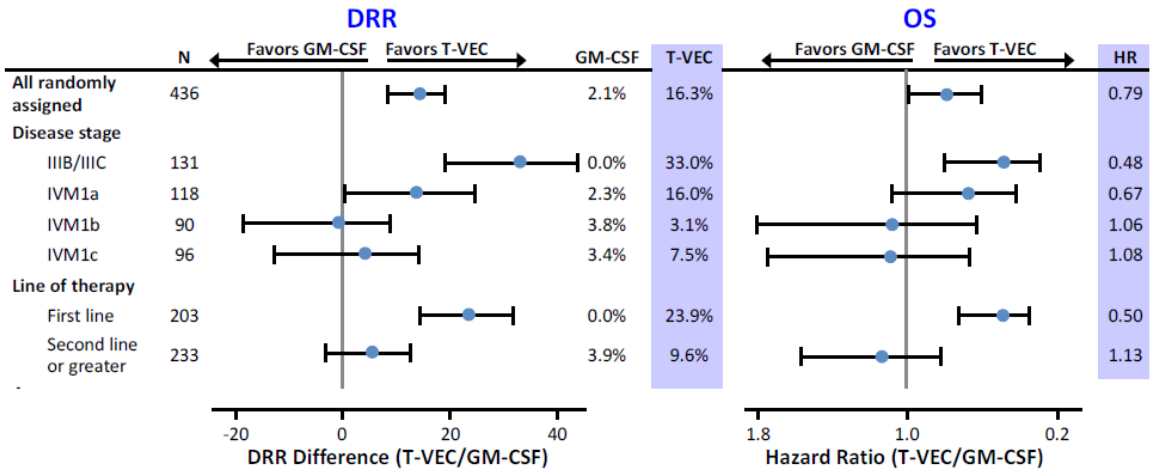
• The absence of a clear effect on overall survival;

• Limited evidence that the product has a systemic effect.

Rapid Change in Melanoma

Talimogene laherparepvec is a replication-competent virus derived from an attenuated Herpes Simplex Virus-1 isolate.

Figure 11. Forest Plot (Hazard Ratio) for Overall Survival: Key Stratification Factors and Covariates (Study 005/05, Intent to Treat Population)



Source: ODAC Briefing Documents

This is the first such virus to come to FDA's attention. However, other treatments based on viruses are in development. One trial, at Duke University, which uses the polio virus to trigger the patients' immune response to eradicate glioblastoma tumors, was the subject of a recent piece on the CBS show 60 Minutes.

Decisions made in the case of T-VEC will set precedent for subsequent applications.

Amgen's virus is presumed to behave similarly to wild type HSV-1, which means it's likely to demonstrate viral shedding and potential transmission and latent reactivation. The agent is produced through deletion of the viral gene coding for ICP34.5, which reduces neurovirulence compared to wild type HSV-1, and contributes to tumor-selective viral replication.

According to Amgen, deletion of the gene for ICP47 (the antigen processing inhibitor encoded by HSV-1) prevents down-regulation of antigen presentation molecules and increases the expression of the HSV US11 gene, which enhances viral replication in tumor cells.

In the T-VEC case, agency officials and advisors noted that viral shedding may expose healthcare providers and close patient contacts to the engineered virus. In a small number of cases, wild type HSV-1 enters the central nervous system, producing meningoencephalitis, or disseminates and causes multi-organ disease competent virus.

The Amgen application was based on a randomized, phase III study, where subjects in the experimental arm received intralesional injections of talimogene laherparepvec and subjects in the control arm received subcutaneous injections of granulocyte-macrophage colony stimulating factor.

The study—called Study 005/05—was open-label.

In 2:1 randomization, 295 patients enrolled in the talimogene laherparepvec arm and 141 in the control arm. The primary endpoint was durable response rate, defined as CR or PR maintained for at least six months, and beginning at any point within 12 months of initiating therapy.

Overall survival was a secondary endpoint, and no statistically significant result was reached.

There was no question that the virus had a statistically significant higher durable response rate, including complete or partial responses maintained for at least six months, compared with subjects who received GM-CSF.

FDA concurred on the study protocol as part of a Special Protocol Assessment in 2008, documents show.

However, multiple therapies have been approved over the ensuing seven years.

"Since Study 005/05, products approved for the treatment of patients with unresectable or metastatic melanoma and BRAF V600E mutations include vemurafenib, dabrafenib, and trametinib," FDA's questions to the advisory committee state. "The BRAF mutation status is known for only 31 percent of the subjects in Study 005/05.

"Therefore, the extent to which the Study 005/05 results are based on a disease population that now has an alternative of the BRAF inhibitors is unclear."

The take-home lesson for drug sponsors?

If you have the agency's green light for a protocol, hurry up and finish the trials before the science changes.

See the table of FDA-approved therapies for advanced melanoma on page 3.

Agency Pressed for Vote on Traditional Approval

The second lesson is even more generalizable to other applications: if you want an accelerated approval to be an option, make a case for it for it.

Subset analyses showed that T-VEC was more effective in superficial, as opposed to visceral, disease.

According to the company's data, the subsets in which the agent was especially effective were Stages IIIB/IIIC and IVM1a. See Figure 11 on page 4.

Though Amgen sought full approval, company officials said in the presentation that they would open to discussion of an accelerated approval. (The agency's now refers to full approval as "traditional.")

FDA's questions to the advisory group state that Amgen's BLA contains no rationale for an accelerated approval, which would require demonstration of impact on a surrogate endpoint:

"FDA has the regulatory flexibility to consider this BLA for either traditional approval or accelerated approval," questions to the advisory committee state. "FDA could approve the product under the accelerated approval pathway for either the proposed indicated population, or for a subgroup of the proposed population.

"However, the BLA submission does not contain any statements from the applicant regarding how the available data might support accelerated approval. In the absence of a submission that presents the applicant's position regarding accelerated approval, and the absence of FDA review of such a submission, a full and fair consideration of the accelerated approval pathway for use of talimogene laherparepvec is not feasible at the time of this advisory committee meeting.

"For this reason, although the committee discussion may include consideration of accelerated approval, FDA asks the committee to vote only on the question of traditional approval for talimogene laherparepvec."

Several advisors asked FDA staff whether it would be possible to rephrase the question and suggest an accelerated approval, which would be conditional on post-approval studies, but they were told that the agency first wanted a vote on a traditional approval.

This stance channeled the committee's discussion toward tradition approval. The advisors ended up voting up or down on what amounted to a cluster of questions, which created rifts that didn't need to be there. Instead of unambiguous votes, the agency ended up with hours of discussion.

After the vote for traditional approval was taken, the option of an accelerated approval was rendered moot.

Before the vote, Celia Witten, director of the CBER Office of Cellular, Tissue and Gene Therapies, said that based on precedent, the agency would need to establish that the agent has a systemic effect if it is to be seriously considered for an accelerated approval.

"When we ask you about benefit, we are really interested in knowing whether there is a direct benefit to patients from this response that they've seen," Witten said. "Accelerated approval is something the committee is free to discuss, but one thing to keep in mind is that in drugs that have been approved based on response rates there is an understanding that those have a systemic effect.

"If you see a response, you assume that going along with that there is a systemic response experienced by the patient that may be reasonably likely to predict an actual benefit to patients.

"That's why in this case we brought out the issue of to what extent there is or isn't evidence of a systemic response. We would really appreciate a discussion of the benefits question. Or if they think it's a surrogate, we would like to understand it especially in view of this difference in the mechanism between this product and other things that have been approved based on response.

"There is also a question of patient population. For somebody to be in the accelerated approval pathway, they would have to provide a meaningful advantage over available therapies.

"We don't have a lot of [data] about surrogates or meaningful advantage over available therapies, because that's no what was presented to us in the BLA."

Subsets and the Value of Local Control

NCI's Sherry, who served as a temporary voting member, said he was unconvinced "by what the sponsor calls 'clear evidence of systemic effect of T-VEC.'"

Said Sherry: "Here we get into the area of survival, we get into the area of risk of death, we get into the area of uninjected visceral disease, we get into the area of potential benefit based on the stage.

"The response of non-injected sites is soft at best. There is no evidence that visceral metastases respond. And non-visceral metastases clearly can respond.

"From the clinical benefit perspective, it seems to be best characterized by saying, 'If you can inject it, there is a pretty good chance it's going to go away. And if you can't inject it, you have to be really cautious about how you interpret that and what you do about that abnormality.'

"Given that, where this fits in is going to take a really careful consideration of patients you select for this."

Through most of the meeting, Sherry clashed with Patrick Hwu, professor at the Department of Melanoma Medical Oncology at MD Anderson Cancer Center.

"I think what is very clear is that there is response

of injected lesions," said Hwu, also a voting temporary member. "But I want to emphasize that that's really important. Because in the clinic you have patients in this setting who have local disease that can be disastrous if you don't get on top of that. That disease continues to grow, it becomes malodorous. It's just a horrible situation.

"I want to make sure that we don't overlook that durable response of an injected lesion is actually an incredibly helpful thing for patients. Even patients with liver mets. Patients can't see their liver mets.

"A lot of patients have a liver met, but the one they are concerned about and really bothers them is the one that they can see. Just being able, from a psychological point of view, to get rid of that one is an important endpoint."

Another member of the committee, Richard Simon, chief of the NCI Biometric Research Branch, said he found the sponsor's subset analysis compelling.

"It's substantial evidence that it's basically the skin lesions and the nodal lesions that are showing response, and the survival data there is very strong data that patients with visceral involvement do not have the survival effect and there seems to be surprising survival benefit in patients without visceral involvement," Simon said.

However, Simon said he would feel more comfortable "if it were restricted to patients who didn't have visceral metastases."

The dose of the agent is also unclear, in part because of variability of surface lesions. In the pivotal trial, a lot was left to the physician's discretion, and as a result lesions received variable doses.

There was no documentation of the patient's self-reported assessment of benefit.

The Significance of the Word "Unresectable"

The approval question presented to the committee differed from the criteria for Amgen's pivotal trial.

The word "unresectable," present in the trial's title, was missing from the approval question:

• **The trial:** The objective of this study is to evaluate the efficacy and safety of treatment with OncoVEX GM-CSF compared to subcutaneously administered GM-CSF melanoma patients with unresectable Stage IIIb, IIIc and Stage IV disease. The efficacy endpoints of the study aim to demonstrate overall clinical benefit for patients treated with OncoVEX GM-CSF as compared to GM-CSF.

• **The Approval Question:** Does talimogene laherparepvec have an overall favorable benefit-risk profile for the treatment of injectable regionally or distantly metastatic melanoma? In voting, please consider only whether the available evidence would support traditional approval, not accelerated approval.

If T-VEC has systemic effect, limiting access to patients deemed unresectabe would make no sense, proponents of the therapy argued.

"Although unresectable at baseline, after treatment with talimogene laherparepvec, nine subjects were able to undergo surgery that successfully

resulted in no residual disease," Amgen's application states. "Evidence of a systemic effect of talimogene laherparepvec was demonstrated, with responses observed in both injected lesions and in noninjected lesions (including visceral lesions) on a time course consistent with a delayed, systemic anti-tumor response, as well as a decreased risk of developing visceral metastases in subjects receiving talimogene laherparepvec compared with those receiving GM-CSF."

The company is conducting a 150-patient randomized trial in the neoadjuvant setting.

Most other agents used to treat melanoma are indicated for metastatic *or* unresectable disease.

What would be a disadvantage to keeping the word unresectable in the label, as per clinical trial?

Insurance reimbursement could become a problem, warned Hwu.

"I am just going to talk about the practicality of when something is in the clinic and when we see a patient we have to prescribe the drug," he said. "There are a lot approvals, a lot of people we have to go through, including insurance companies, so when we have something that's wishy-washy in there, then the patients get covered or not get covered based on how things get interpreted.

"And what happens sometimes is we have a drug that we want to give to a patient, but we can't do it, because they would then get a huge bill, because their insurance won't cover it."

Said Sherry: "I agree that resectability is in the eye of beholder. But I think it should actually be kept in. Maybe it can be expanded with words like 'resected for cure.' To leave it out opens Pandora's box of possibilities that for me would not make sense."

Deborah Armstrong, chair of ODAC and professor of oncology at Sidney Kimmel Comprehensive Cancer Center at the Johns Hopkins University School of Medicine, concurred that there would be an advantage to keeping "unresectable" in the label.

"I think leaving it out opens the door to a potential population that hasn't been studied," Armstrong said.

Later, while voting for approve, Armstrong said that she concurred with Sherry's assessment of T-VEC's application.

"I do think it should be limited to the eligibility for

the participation in the 05 Study," she said. "I think it's the group where we have seen the benefit. I wouldn't extend it outside that, but I think there is a benefit for that group as a whole, and I think this should be something in the armamentarium for the people who treat this disease.

"I did think that there needs to be very careful guidance for dosing and administration, and probably something like teaching videos, because this is not going to be an easy thing for staff to pick up and learn."

Hwu said physicians should be allowed to decide how this therapy should be used:

"[Data] show that there is a special benefit for the [Stages IIIB/IIIC and IVM1a], which is still nasty disease, and you have to take care of that. You would probably five them an anti-PD1 first. If you want to look, from a clinician's point of view, all of the wonderful drugs that are out there, you also have to look at all the wonderful toxicities that they bring.

"How would we actually use this, from a clinician's point of view, I think if I had a [Stage IIIB or IIIC] patient, I would probably put them on a PD-1, but a lot of patients don't respond to that stuff. In fact, the majority of patients don't respond to that. And then what do you do? If they had a cutaneous lesion that was really bothering them at that point, I would put them on [T-VEC].

"I think this is a very reasonable agent to try to utilize. I don think we are keeping anyone from getting a PD-1."

Arrow in the Quiver?

Before the question came up to a vote, Hwu and Sherry sparred directly on selection of appropriate patients for the agent and the potential of steering patients away from systemic treatments from which they are more likely to benefit:

SHERRY: Let me ask you a question: If you had a 60-year-old guy, and he's got two liver lesions and two lung lesions, and six months ago the scans looked okay. And he has a 2-centimeter right groin node. Good health. Would you ever consider this as front-line therapy, and if you would, in what circumstances?

HWU: I think we already decided we are not going to talk about front-line, second-line, third-line, because we don't have the data for that.

SHERRY: Just help me clarify that.

HWU: In my clinic, if someone can walk in, I usually give them an anti-PD-1 first. That's just what I do. It's got low toxicity, it's got decent efficacy. It's what you would get if you walked into my clinic.

SHERRY: Is there any circumstance…

HWU: But, Rick, I have huge numbers of patients that [PD-1] doesn't work in. And they still come back to you, you know…

You might send them back to the regular place at NCI, but we actually keep following them, and then we have to come up with something else for them. Those patients need something, and I need as many arrows in my quiver to give to that patient as possible.

And when you are out of those arrows, what can you then do for that patient?

It may not be upfront, but I can see that patient that you described getting that agent at some point.

SHERRY: So does it further the discussion or weaken the discussion not to step up to the plate and define whom this makes sense in?

You can't just leave it open. And that 60-year-old guy, if he walks into some clinic, he could get T-VEC, and I think that we know enough to know that is not a good choice.

And it seems to me that not to say that and to not let people know that is a mistake.

HWU: I don't think we have the information yet to micromanage the series of what you get first. Clearly, I have my opinions, but in the end they are my opinions about what I give first.

I give everyone an anti-PD-1 first. But that's just my opinion. That study has not been done yet. The studies need to be done, and I don't think this study was designed to answer that question, and my suggestion is not to narrow it in the way that it wasn't designed to narrow.

SHERRY: Not to be flip, but Daniel Moynihan once said that everybody is entitled to their own opinion, but not their own set of facts, and the facts clearly show that there is no reproducible benefit in the setting of metastatic disease.

Can I conjure up something for that it would make sense? Absolutely.

If they've seen other therapies, they have bad disease, or it's in combination—absolutely.

But to think that this could be presented in an acceptable fashion as front-line therapy to healthy individuals just floors me. If this is going to be approved for the indication that was in this briefing, which includes patients who had brain metastases, resected, and three liver lesions, and unlimited number of pulmonary lesions as stand-alone front-line therapy,

that's just not acceptable.

You could do it in conjunction with something. You could add something to actually give that patient a chance to have an objective regression of the disease that we know is going to kill him or her, than that's a different situation.

But as a stand-alone treatment it makes no sense.

Safety Profile

FDA's briefing documents summarize the agent's safety profile:

• 90 percent of subjects who received talimogene laherparepvec experienced "flu-like symptoms."

• The most common treatment-emergent adverse events with talimogene laherparepvec were fatigue, chills, pyrexia, nausea, influenza-like illness and injection site pain.

• 63 percent of subjects experienced adverse events that were Grade 1-2, and 37 percent subjects experienced adverse events Grade 3 or above in the talimogene laherparepvec arm.

• The incidence of treatment-emergent adverse events, regardless of severity, was greater in the talimogene laherparepvec arm than in the control arm.

• Cellulitis at the injection site, impaired wound healing, herpes simplex-1 infections, injection site reactions, and vitiligo were identified by the applicant as adverse events of special interest for subjects who received talimogene laherparepvec.

• After talimogene laherparepvec administration, a wound became resistant to medical therapy, and required a below-the-knee amputation.

• Immune-mediated events occurred in both arms. Four of six such events (glomerulonephritis [n=2]; vasculitis [n=1], and hypothyroidism [n=1]) were de novo after talimogene laherparepvec therapy.

• Disease progression was the most common Grade 3 or above adverse event, the most common reason for early discontinuation, the most common treatment-emergent serious adverse event, and the most common preferred term for treatment-emergent fatal event.

Congress Narrows Down 21st Century Cures Proposal

(Continued from page 1)

In addition to boosting NIH funding by $10 billion over five years and establishing a clinical trial data system for federally funded trials, the discussion draft includes provisions for developing the next line of antibiotics.

The bill includes a "placeholder"—a promise of language that will come later—for providing incentives for repurposing drugs for serious and life-threatening diseases and disorders.

The bill would require FDA to create a priority review program for breakthrough medical device technologies. A section of the draft legislation aims to provide clarity for developers of software products used in health management and medical care.

"It has become increasingly clear in recent years that our regulatory policies have not kept pace with innovation and there is much more we can be doing to provide that hope to folks. That's what this bill does," Upton said at a legislative hearing of the Subcommittee on Health April 30.

"This discussion draft, the product of eight hearings, more than two-dozen roundtables, and several white papers, incorporates the patient perspective into the regulatory process.

"It will increase funding for NIH. It modernizes clinical trials, including allowing for more flexible trial designs so we can customize trials based on the unique characteristics of patients most likely to benefit. 21st Century Cures will unlock the wealth of health data available so patients, researchers, and innovators can communicate and keep the cycle of cures constantly moving and improving."

A section-by-section summary of the 200-page discussion draft, produced by the House committee, is available here.

Advocates: "A Major Step Forward"

The legislation builds on an earlier version of the discussion draft released Jan. 27, said Jon Retzlaff, managing director of science policy and government affairs at the American Association for Cancer Research (The Cancer Letter, Jan. 30).

"In this new discussion draft bill, we are especially encouraged that the leaders on the Committee have prioritized NIH funding by recommending significant annual budget increases for the NIH, including the proposal for $10 billion over the next five years in

mandatory funding through an NIH Innovation Fund.

"Ever since Chairman Upton and Congresswoman DeGette introduced the 21st Century Cures initiative one year ago, it has been a priority both for the AACR as well as others in the medical research community, to advocate for the inclusion of authorization language to ensure robust and sustainable (over the long-term) NIH annual funding increases," Retzlaff said to The Cancer Letter. "Therefore, we applaud the fact that the leaders have come together in a bipartisan manner to make this happen."

The American Society of Clinical Oncology is reviewing the legislative draft, said ASCO Chief Medical Officer Richard Schilsky.

"ASCO is encouraged by the bipartisan efforts of members of the House Energy and Commerce Committee to fully examine and develop policies for improving the way we translate research and innovations into improved medical care," Schilsky said in a statement.

"One provision we are particularly pleased with calls for $10 billion in mandatory funding for a National Institutes of Health Innovation Fund over the next five years. Research funding is the bedrock of advancing medical care and we are pleased that the committee leadership has made this a priority.

"We congratulate the committee leadership on the release of this draft and look forward to working together once we have an opportunity to fully review it."

Upton and DeGette kept their promise to increase funding for research, said Research!America President and CEO Mary Woolley.

"We're thrilled that members of Congress came together on a bipartisan basis to take the next step with this important initiative to accelerate the discovery, development and delivery of lifesaving treatments for patients," Woolley said in a statement. "Chairman Fred Upton and Representative Diana DeGette have maintained from the beginning that they would boost funding for medical research, and they followed through with a $10 billion increase for the NIH over five years in this legislation.

"While it is important for the final language in the bill to allow for flexibility in the use of these funds in order to maximize their benefit, these additional dollars can empower NIH to sustain and embark on innovative studies that could reduce the prevalence and impact of costly and disabling conditions that continue to threaten individual and population health, our economic security, and global competitiveness.

"FDA also requires additional resources to fulfill new responsibilities outlined in the bill. We look forward to reviewing the many other important provisions in this bill and offering input as the committee process moves forward."

No Additional Funding for FDA

The draft, however, does not recommend funding increases for FDA.

"On the flip side, we are extremely concerned that the committee's discussion draft bill does not recommend any budget increase for FDA even though the bill proposes that the agency carry out a whole host of additional responsibilities that are specified in the discussion draft bill, including updating or issuing more than 15 guidance documents and implementing a variety of new programs and processes across numerous disease areas," Retzlaff said. "We cannot just continue to ask the FDA to take on more responsibilities with fewer resources.

"Therefore, it is top priority for the AACR to ensure that the next iteration of the 21st Century Cures' discussion draft bill also includes a recommendation for strong annual funding increases for the FDA so that its outstanding staff is able to continue to review potential lifesaving drug and new product applications in a timely manner while also carrying out some of the additional statutory requirements that have been proposed.

"In fact, we will be providing an in-depth and comprehensive analysis of the full text of the 200 page discussion draft bill over the next week to members of the AACR Science Policy and Government Affairs Committee so that a more thorough and complete response from the AACR will be shared with Members and staff from the House Committee on Energy and Commerce."

The committee will continue to work on regulation of diagnostic tests and telemedicine, said Health Subcommittee Chairman Joseph Pitts (R-Pa.) at the April 30 hearing.

"With respect to diagnostics, we remain absolutely committed to developing a modernized regulatory framework for these innovative and increasingly important tests and services," Pitts said. "Understanding this is a particularly unique and complex endeavor, we look forward to working in a deliberative manner over the coming weeks with Dr. [Jeff Shuren, director of the FDA Center for Devices and Radiological Health] and stakeholders to advance legislation.

"On telemedicine, I continue to work with my colleagues in the Energy and Commerce Working

Group on Telemedicine toward a bipartisan proposal that will encourage the use of telemedicine services to improve health care quality and outcomes, increase patient access, and control costs. I want to thank the administration and CBO for their input and look forward to our continued collaboration moving forward."

Institute of Medicine to Become National Academy of Medicine

The membership of the National Academy of Sciences voted April 28 at its 152nd annual meeting to change the name of the Institute of Medicine to the National Academy of Medicine, effective July 1.

The National Academy of Medicine will continue to be an honorific society and will inherit the more than 1,900 current elected members and foreign associates of the IOM.

The National Academy of Medicine will join the National Academy of Sciences and National Academy of Engineering in advising the nation on matters of science, technology, and health.

IOM President Victor Dzau will serve as the first president of the National Academy of Medicine.

"This change recognizes the important achievements of medical and health researchers, clinicians, and policymakers in improving health and medicine both nationally and globally," Dzau said. "We look forward to expanding our work together with the other Academies, and I am confident that this development will enhance our ability to provide evidence-based advice aimed at improving the lives of people everywhere."

According to IOM, this change is part of a broader internal reorganization to more effectively integrate its work with the other national academies. Reports and studies on health and medicine will continue uninterrupted as activities of the Institute of Medicine, which will become one of the six program units operating under the direction of the integrated academies.

"The establishment of the National Academy of Medicine is a significant milestone in our history," said NAS President Ralph Cicerone. "It is an acknowledgement of the importance of medicine and related health sciences to today's global research enterprise. It will also better align us to take a more integrated, multidisciplinary approach to our work, reflecting how science is best done today."

C.D. Mote Jr., president of the National Academy of Engineering, added: "Today, science, engineering, and medicine share many common areas of interest in the pursuit of discoveries, advancing knowledge, and solving problems of people and society. Having three national academies under one roof shows the ongoing collaboration among the people who are tackling today's grand challenges."

The National Academy of Sciences was founded in 1863 under a congressional charter signed by President Lincoln, which created a body that would operate outside of government to advise the nation "whenever called upon." The National Academy of Engineering was founded in 1964. The Institute of Medicine was established as the health arm of the NAS in 1970.

Letter to the Editor

MD Anderson Administration Behaves as a "Financially Privileged Elitist Group"

To the Editor:

Congratulations on your outstanding article entitled "MD Anderson Execs Get Big Raises In the Midst of Faculty Morale Woes." As a 35-year faculty member of the MD Anderson Cancer Center, now retired, I am deeply disturbed at the endangered reputation of one of the greatest institutions of its kind in the world. Every other month seems to bring some embarrassing new revelation at the hands of the current leadership. Last month, it was a scathing report by the American Association of University Professors (AAUP) that excoriated MD Anderson administration for disregard of well-established principles of academic freedom and shared governance. This month it is $251,000 and $322,000 compensation increases for two administrators, each already rewarded to the tune of over $1 million per year. This latter issue would be controversial at the best of times, particularly for state government employees, but with dwindling cancer research dollars, increased performance demands on medical and research staff, rock-bottom faculty morale, and the financial worries of suffering cancer patients and their families, it is near unconscionable. I write to clarify some comments made by MD Anderson administration regarding these issues.

One of the questions posed by the Cancer Letter to MD Anderson officials was: "Are controls in place to ensure MD Anderson is transparent about executive salaries and that the institution receives appropriate approvals from the university system for salaries?"

The response was: "Yes, there are several controls. In fact, when researching this story, you saw some of these controls. Administrative Accountability Reports are annual reports required by the state of Texas to track leader salaries at institutions across the state and to ensure pay structures are appropriate. In addition, UT System approval is required when total proposed compensation for an employee will be over $500 thousand. Board of Regents approval is required when total proposed compensation is over $1 million."

Either the MD Anderson leadership team does not understand the requirements of the Texas Administrative Accountability Reports or have deliberately misrepresented them. The reports became law as a rider (Number 111) to House Bill 1, the General Appropriations Act of the 78th Texas Legislature, and took effect in June 2003. They have absolutely nothing to do with executive salary "controls." Likewise, they have nothing to do with "ensuring pay structures are appropriate." By what convoluted logic could MD Anderson leadership possibly reach that conclusion? The "accountability" component of the reports relates solely to transparency. This legislation mandates that the name, salary, percent salary increase, and total value of non-salary benefits of high-ranking administrative officials in Texas state higher-education institutions be reported to various state agencies by Dec. 1 of every fiscal year, and that a copy of the reports be made available for public inspection, not later than seven days after submission, in the library of each institution. Failing such action, appropriated state funds may not be spent. That is the full extent of the accountability requirement. Nothing more. Nothing less. Rider 111 to House Bill 1 can be found here.

The approval required by UT System when the total proposed compensation for an employee is over $500,000 or by the Board of Regents when it is over $1 million is substantially pro forma. What percent of such compensation requests by MD Anderson administrators have ever been turned down, even in the face of overwhelming evidence of collapsed morale in the constituencies they profess to serve? But that's a different letter.

In the context of correcting false claims, consider the following statement attributed to Mr. Dan Fontaine, executive chief of staff at MD Anderson during an interview with Modern Healthcare on MD Anderson's term-appointment renewal problems and the involvement of the AAUP: "Fontaine also pointed out that the association's report stated that patient care had not been compromised as a result of the dispute, which he expects will die down soon."

The report contains no such statement. The AAUP investigating committee was not charged with evaluating the quality of patient care and, indeed, had neither the collective experience nor the necessary access to appropriate MD Anderson personnel and data resources to address it. Far from supporting Mr. Fontaine's claim, the AAUP report cites two surveys which indicate that patient care has been compromised at MD Anderson under the current administration. In a September 2013 in-house survey, 56 percent of 548 faculty respondents agreed that "demand for increase in clinical productivity negatively impacted patient safety," and 69 percent agreed that "increased clinical demands affected [their] ability to provide optimal patient care." In a subsequent survey, conducted by the University of Texas System in September 2014, only 39 percent of clinical faculty respondents were satisfied with progress or improvements in patient safety, while 60 percent were dissatisfied with "clinical productivity expectations." Previously reported in the news media, these findings are far too important for the well-being of the citizens of Texas and the nation to be marginalized in the name of political expediency. As decreed by the Texas legislature, "The people do not give their public servants the right to decide what is good for the people to know and what is not good for them to know."

During a recent visit to MD Anderson Cancer Center, UT System Chancellor William McRaven acknowledged that trust was broken between MD Anderson administration and faculty, and pledged to address it. That is an admirable and reassuring commitment, particularly from a leader of Chancellor McRaven's stature. But as long as MD Anderson administration is allowed to behave as a financially privileged elitist group with license to disseminate false or misleading information, either knowingly or neglectfully, such trust can never be established. Given the ever-growing list of controversial behaviors of some MD Anderson executives, it is clear that Chancellor McRaven is confronted with a daunting "special operations" challenge—even for a tough, resourceful, and accomplished former Navy SEAL Commander.

David Farquhar
Emeritus Professor of Cancer Medicine
MD Anderson Cancer Center.

An Appreciation

Mike Katz, 61, Advocate, Educator

By Michael D. Scott

The cancer field is filled with advocates—advocates for research into specific forms of malignancy, advocates for access to care for patients with limited resources, advocates for pediatric cancers—you name it. Many of these people are motivated, passionate, determined, and successful in moving their specific agendas forward in the interests of patients, clinicians, researchers, and others.

But even within this motivated and passionate group of people, Mike Katz was a special individual who stood out. And he explained it this way:

"I've always chosen to live my life as if I didn't have cancer. I just face forward and try to do everything I want to do, working around symptoms and treatment side effects," he said. "I've been a patient for so long, I'm much better now at managing those things."[1]

Diagnosed in 1990 at just 37 years of age with an iliac plasmacytoma that was causing weakness in his right leg and a consequent limp, he wasn't initially told in any detail about the myeloma. His doctors were focused on the orthopedic problem and (again in Mike's own words), "with the Internet still in its infancy, there were no online patient support groups or myeloma advocacy organizations to turn to for information."

It was 18 months before Mike's myeloma began to progress and he learned that an allogeneic bone marrow transplant (ABMT) might be wise. In 1992 myeloma was associated with a survival time of three to five years, and the overall mortality rate for an ABMT was between 25 and 50 percent. Mike had a head for statistics, and like the good researcher that he always was, he set out to "do his homework." Along the way he met with the late Francesca M. Thompson—a highly regarded specialist in orthopedics. Dr. Thompson had written about her own struggle with myeloma,[2] based on her experience as one of the very earliest patients to have an ABMT for myeloma. She not only helped Mike to decide what needed to be done to treat his own myeloma and its associated bone lesions, she also set him—inadvertently—on a course that would change his life.

"The impact of talking with Dr. Thompson," said Mike, "was so powerful, and I felt so grateful, it got me thinking that I could do the same for others."

From that point forward, Mike became one of the most widely known myeloma patients in the world.

Mike Katz

It is impossible here to document all of his efforts to help others diagnosed with this form of cancer, but his efforts went far beyond that:

He worked with the International Myeloma Foundation (IMF) to set up their patient database.

He spoke as a patient for years at the IMF's Patient & Family Seminars.

In 1995 he worked with others to build a web site for the IMF, which, for the very first time, allowed newly diagnosed patients from all around the world to gain knowledge and information about their disease within days of their initial diagnosis – and revolutionized access for patients to detailed knowledge and resources.

He founded an online myeloma discussion forum through the Association of Cancer Online Resources (ACOR), which he moderated for the rest of his life.

And then he realized that he could do more:

He became a patient advocate with the Eastern Cooperative Oncology Group (ECOG).

He was elected to be the Chair of ECOG's Patient Representative Committee.

He became Chair of the Coalition of Cancer Cooperative Groups' Patient Advisory Board.

He was appointed to and became Chair of the Director's Consumer Liaison Group at the National Cancer Institute.

He participated in the Drug Development Patient Consultant Program at the U.S. Food and Drug Administration.

Meanwhile, at every annual meeting of ASCO and ASH for the past many years, Mike could be found in the IMF's booth in the conference exhibit hall, where he conducted video-interviews about newly presented myeloma research with experts and researchers from all over the world—and many of those clinicians and researchers thought of those interviews as one of the highlights of the meeting.

And he was doing all of this while still holding his job as a partner and vice president with the New York-based consulting firm of Booz Allen.

But there were two other things of which Mike was particularly proud, even though he rarely mentioned them himself.

In 2004, after there had been multiple case reports of onset of osteonecrosis of the jaw (ONJ) among patients being treated with bisphosphonates for myeloma, Mike worked with others to survey over 1,200 patients (most with myeloma but nearly 300 with breast cancer). They showed that among the patients with ONJ (or showing symptoms suspicious for this condition), 71 percent had been treated with zoledronic acid and the other 29 percent had been treated with pamidronate.[5] Few cancer advocates have ever got their names as an author on a research paper in the New England Journal of Medicine. These findings led to changes in the prescribing information for the bisphosphonates as a class, and to changes in clinical practice guidelines for the use of the bisphosphonates.

Slightly earlier, he had persuaded the Chair of the ECOG Myeloma Committee to conduct a randomized, comparative trial (E4A03) of low-dose vs. standard-dose dexamethasone, along with lenalidomide, in the first-line treatment of newly diagnosed myeloma, based on his personal experience of using low-dose dexamethasone, along with the experience of other patients with whom he had been communicating. The clear survival benefit in this trial (initially reported at the ASCO annual meeting in 2007),[3,4] and the reduction in adverse events, favored the low-dose dexamethasone regimen. This not only revolutionized the first-line treatment of myeloma, it also led to radical changes in the dosing of dexamethasone in almost all cancer regimens requiring the use of this corticosteroid.

At the annual meeting of ASCO in 2014, Mike was deservedly recognized—very much to his own surprise—with the ASCO Partners in Progress Award for his contributions to cancer awareness and public advocacy. He will be widely missed, not just by his family and friends, but by all in the myeloma community and by many, many people across the cancer community as a whole.

Mike died on Sunday, April 26, on Long Island, from complications associated with multiple myeloma, with which he had lived for a total of 24 years—an unheard of survival time in 1990, when he was initially diagnosed. He quite certainly benefitted from the several new drugs that have been added to the myeloma armamentarium over the past 15+ years, and he participated in early clinical trials of several of these agents. He had also been diagnosed with and successfully treated for colon cancer along the way.

He is survived by his wife, three sons, and seven grandchildren. He will be remembered as a colleague, friend, mentor, adviser, and someone who would invariably go the extra mile to help others. While he could certainly "speak his mind" when he felt he needed to, nothing was ever about him; almost everything he did was done to help others. He will also be remembered for his passion for opera, his involvement as a lay leader at his synagogue on Long Island, and his volunteer work for Lifeline for the Old, an organization in Israel that provides employment and social services for the elderly.

The author is a member of the board of directors of the International Myeloma Foundation.

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Stories About Mike Katz:

• Officials Open to Fine-tuning Group Budgets as Advocates Chip Away at NCTN's Façade (The Cancer Letter, May 2, 2014)

• ASCO 2014: Special Awards (The Cancer Letter, May 30, 2014)

• Reviews of the [MD Anderson] Faculty Report by Irwin Krakoff, Robert Cook-Deegan, and Michael Katz (The Cancer Letter, March 29, 2013)

In Brief

Margaret Kripke to Step Down As CPRIT Chief Scientific Officer

(Continued from page 1)

"I also wanted to make sure that CPRIT's investments in cancer research were strategically directed to some underfunded areas where there was opportunity for progress, such as prevention, early detection, and childhood cancers.

"I'm pleased to say that CPRIT is now flourishing, the research program is making rapid progress, priority areas for research have been established, and so I feel that I have accomplished what I set out to do.

"It seems like a good time for me to allow someone else to take on the responsibilities of being CPRIT's chief scientific officer. I'll do whatever I can to make sure there is a smooth transition and expect to remain a strong supporter of CPRIT and its mission."

Kripke, 71, will retire as soon as the agency can find a successor, no later than Aug. 31.

"CPRIT is now hitting its stride due in large part to Dr. Kripke's leadership of the academic research program," CPRIT CEO Wayne Roberts said to The Cancer Letter. "The one person I credit with CPRIT's turnaround is Margaret Kripke.

"She recruited and retained eminent peer reviewers who will help launch the next chief scientific officer. Dr. Kripke identified early detection, intractable and rare cancers, especially pediatric and juvenile cancers, to become board adopted agency priorities.

"Everything CPRIT is today is part of her legacy to Texas. The board and I are happy Margaret gets to resume her retirement, but we'll miss our daily interaction with this cherished colleague."

According to CPRIT, Kripke brought "tremendous credibility" to the institute as the former executive vice president and chief academic officer of MD Anderson, anchoring the agency's research program during its restart after Senate Bill 149 (The Cancer Letter, Dec. 14, 2012). http://www.cancerletter.com/articles/20121214

"She reconstituted the research panel peer review process with amazing experts from around the country," CPRIT said in a statement.

The agency approved a $125,000 contract April 27 with Spencer Stuart, an executive search and leadership consulting firm to recruit Kripke's successor.

CPRIT was launched in 2009, after a bond issue to fund the program was approved by voters in 2007. To date, CPRIT's 868 awards have invested $1.24 billion in cancer research.

"Margaret stepped into a very difficult situation and put her scientific reputation on the line to help restore the credibility of CPRIT in the eyes of the Texas State Legislature," said Ted Yank, associate director for administration of the Dan L. Duncan Cancer Center at Baylor College of Medicine. Yank has been involved with the creation of CPRIT from the beginning—reviewing legislation, participating in oversight committees, and coordinating Baylor's responses to CPRIT.

"She conducted herself with grace, professionalism and took an ecumenical approach that achieved that goal," Yank said to The Cancer Letter. "Anyone with stake in this tough fight against cancer owes her a debt of gratitude."

THE CANCER PREVENTION AND RESEARCH INSTITUTE OF TEXAS awarded two grants through its academic research program. The grants, totaling $6,000,000, support the recruitment of two top cancer scientists to academic institutions in Texas.

The awarded grants include: $2 million for the recruitment of **Margarida Santos** to MD Anderson Cancer Center from NCI; and $4 million for the recruitment of **Xiaochun Yu** to the University of Texas Southwestern Medical Center from the University of Michigan Medical School.

THE AMERICAN SOCIETY OF CLINICAL ONCOLOGY Conquer Cancer Foundation announced the recipients of the 2015 Merit Awards, Oncology Travel Trainee Awards, Medical Student Rotation Awards and Resident Travel Awards.

The Merit Awards support clinical cancer researchers early in their careers by providing them with the opportunity to present their research at ASCO's annual meeting. This year the Conquer Cancer Foundation is honoring 100 young oncologists for the research they will present at the 2015 ASCO Annual Meeting.

The full list of 2015 Merit Award Recipients is available at www.conquercancerfoundation.org. Four recipients will be presented with Special Merit Awards for receiving the highest ranking scores in their respective abstract categories, as determined by the ASCO Scientific Program Committee:

• **Maria-Jose de Miguel-Luken**, of The Institute of Cancer Research and The Royal Marsden Hospital, will receive the Bradley Stuart Beller Award for the

highest ranked abstract by a fellow, resident or trainee: "A pharmacokinetic and pharmacodynamic biomarker-driven phase I study of intermittent, low dose intensity schedules of the dual MEK/RAF inhibitor, RO5126766 (RO) in patients (pts) with advanced solid tumors."

● **Mark Applebaum**, of the University of Chicago, will receive the Brigid Leventhal Award for the top-ranking abstract in pediatric oncology: "Second malignancies in neuroblastoma patients: A report from the International Neuroblastoma Risk Group."

● **Sébastien Héritier**, of Versaille University & APHP, Trousseau Hospital, will receive the James B. Nachman Award, which is given to a junior faculty member in pediatric oncology: "Langerhans cell histiocytosis in children: Correlation of BRAF status with clinical characteristic."

● **Ryan David Nipp**, of Dana-Farber Cancer Institute/Harvard Cancer Center, will receive the Pain and Symptom Management Award for the highest-ranked abstract in pain management research: "Quality of life and mood in patients with advanced cancer: Associations with prognostic understanding and coping style."

Additionally, the foundation is providing 64 Oncology Trainee Travel Awards this year. These awards support the continuing education and professional development of trainee oncologists by providing them with a complimentary 2015 annual meeting registration, as well as an individual travel grant for expenses to and from the meeting.

The Medical Student Rotation Award for Underrepresented Populations and the Resident Travel Award for Underrepresented Populations provide opportunities for young researchers of diverse backgrounds to forge their way in the oncology field.

The Medical Student Rotation Award provides clinical or clinical research oncology rotations for U.S. medical students and pairs students with oncologists for academic and career mentorship.

The 2015 recipients are:

● **Oladapo Adeniran**, University of Illinois at Chicago
● **Cecil Benitez**, Stanford University
● **Mario Martinez**, University of Illinois at Chicago
● **Angel Moran**, University of California, Davis
● **Dionisia Quiroga**, Michigan State University
● **Elisa Quiroz**, Ponce Health Sciences University
● **Jasmine Smith**, University of South Carolina School of Medicine Greenville

The Resident Travel Award provides financial support for residents to attend ASCO's annual meeting.

The 2015 recipients are:

● **Olufunke Akinbobuyi**, Morehouse School of Medicine
● **Idoroenyi Amanam**, St. Mary Medical Center
● **Ebenezer Appah**, Meharry Medical College
● **Frederick Doamekpor**, Morehouse School of Medicine
● **Nancy Osuji-Oduh**, Morehouse School of Medicine
● **Linnea Perkins**, Ochsner Clinic
● **Sonya Reid-Lawrence**, Meharry Medical College
● **Oluchi Ukaegbu**, Vanderbilt Univ. Medical Center

The 2015 Merit Awards are supported by Amgen; AstraZeneca; Conquer Cancer Foundation Mission Endowment; Gilead Sciences, Inc.; Incyte Corporation; Kidney Cancer Association; Lilly; Novartis Oncology; Onyx Pharmaceuticals; Jackson G. Simpson; Takeda Oncology; and TESARO.

The 2015 Oncology Trainee Travel Awards are supported by Takeda Oncology. The 2015 Medical Student Rotation Awards for Underrepresented Populations is Supported by the Conquer Cancer Foundation Mission Endowment; Eisai Inc.; Genentech BioOncology; and Lilly. The 2015 Resident Travel Awards for Underrepresented Populations are supported by Janssen Biotech, Inc. and Novartis Oncology.

THE BARBARA ANN KARMANOS CANCER INSTITUTE raised more than $2.8 million with its 33rd annual dinner, held at the General Motors Design Dome in Detroit.

The annual dinner chairs were Debra and Bob Ferguson, senior vice president of global public policy at General Motors. Approximately $2.3 million was raised leading up to Karmanos' Annual Dinner, with the event itself raising $500,000 more, which will be used to expand Karmanos's intensive care unit and help create a 24-hour acute care clinic.

This is the fifth consecutive year that a member of GM's senior leadership has chaired Karmanos' annual dinner, which was the first fundraising event to be held in the newly-remodeled GM Design Dome and attracted nearly 600 guests.

Mary Barra, GM's chief executive officer, attended the evening's festivities and paid tribute to her friend, the late Lillian Erdeljan, former Karmanos Cancer Institute board member and long-time Karmanos supporter. She announced that the Erdeljan family was contributing $50,000 to Karmanos' Nursing Department in her memory.

"Lil made so many contributions of her time and resources that ultimately benefitted cancer patients," Barra said. "The ongoing success of the annual dinner is a testament to Lil's immense contributions. It was

her vision, determination and hard work that helped bring the annual dinner to its current status as one of the community's finest and most successful events."

The GM Foundation donated $500,000 for cancer research, supporting Karmanos for the fourth consecutive year. Lear Corp. also showed its generosity by providing a $250,000 match for funds generated by the dinner's live auction and dedicated giving portion.

GM presented unique VIP experience auction packages which included: tickets to the NCAA 2016 Men's Final Four Game; Trump National Golf & Country Club Experience; a Cannes Film Festival Experience; dinner for 10 guests with Steve Kiefer, vice president of global purchasing and supply chain at GM; tickets to the WGC Cadillac Championship; a stay at the Broadmoor Resort in Colorado Springs; a Rolling Stones package; a Cadillac Racing Package; a J Mendel Fashion Package; and an INDY 500 Experience.

The live auction raised more than $367,000, with three packages selling for $100,000 each.

THE INDIANA UNIVERSITY Melvin and Bren Simon Cancer Center raised more than $720,000 for cancer research at its **CHUCKSTRONG Tailgate Gala**, the most in its three-year history.

Hosted by the Indianapolis Colts and head coach Chuck Pagano at the Indiana Farm Bureau Football Center, the gala raised funds through corporate sponsorships and live and silent auctions. The total also included $50,000 given by Pagano and his wife Tina as a matching gift.

"The doctors, the scientists, the researchers, that's who we're honoring tonight," Pagano said. "They're selfless, selfless people. They spend their entire lives trying to find cures for cancer. That's what this event is all about, raising money for cancer research. Our goal is hopefully to find a cure for all blood cancers." In all, the CHUCKSTRONG campaign has raised $2.5 million for research at IU after Pagano was diagnosed with acute promyelocytic leukemia nearly three years ago.

Top-level "touchdown" sponsors for the event were Anthem Blue Cross and Blue Shield, DairyChem, the Efroymson Family Fund, Huntington, Lilly Oncology, and Sol and Kay Raso.

With Colts cheerleaders and more than 50 players, guests at the tailgate gala participated in activities such as a 40-yard dash, punt returns, and tackling stations on the Colts practice field before they turned their attention to raising money for cancer research.

DANA-FARBER CANCER INSTITUTE, the **Harvard T.H. Chan School of Public Health** and the **Irish Cancer Society** formed the Boston-Ireland Prostate Cancer Collaboration, which will conduct and facilitate exchanges of researchers and knowledge between Boston and Ireland.

Researchers from Dana-Farber and Harvard will collaborate with researchers from universities across Ireland, coordinated through the Irish Cancer Society, by participating in periodic teaching and knowledge exchanges with training fellowships and scientific retreats, ultimately resulting in jointly funded high impact projects and published research papers.

With a research infrastructure including an annotated tissue bank and database linking laboratory data, clinical trial findings and patient data outcomes, the initiative will utilize such technologies such as bioinformatics, micro RNA, gene mapping and other tools to support the work.

The program includes a fellowship in which one young Irish scientist or clinician will initially spend a two-year research mentorship in the facilities provided by the Dana-Farber Cancer Institute and Harvard T.H. Chan School of Public Health. The candidate will then return to Ireland to integrate research methods into Irish prostate cancer research practice.

The program will be led by Robert O'Connor, head of research at the Irish Cancer Society. Funding will be provided through grant awards and philanthropic activities and the first fellowship is co-funded by Sanofi-Ireland and Janssen-Ireland.

ST. JUDE CHILDREN'S RESEARCH HOSPITAL and **Novant Health** formed the seventh St. Jude affiliate, to be named the St. Jude Affiliate Clinic at Novant Health Hemby Children's Hospital in Charlotte, N.C., formerly known as Novant Health Blume Pediatric Hematology & Oncology.

Affiliating with St. Jude will give Novant Health Hemby Children's Hospital patients access to more clinical trials than are available at any other facility in the Southeast.

Novant Health Blume Pediatric Hematology & Oncology has offered cancer care to children and young adults in the Charlotte area since 2001.

GEISINGER HEALTH SYSTEM opened its Precision Health Center in Forty Fort, Penn.

The 14,000-square-foot, $562,000 facility will be home to teams from Geisinger's Clinical Genomics and

Autism & Developmental Medicine Institute, and will serve as the primary location for Geisinger Research in northeastern Pennsylvania.

The center will house clinical research space as well as a patient care center with a telemedicine genomics program.

Geisinger is involved in a collaboration with the Regeneron Genetics Center LLC, a wholly-owned subsidiary of Regeneron Pharmaceuticals Inc. This collaboration, announced in January 2014, has already sequenced the exomes of more than 30,000 people, with plans to sequence 250,000 or more. Patients seen for clinical care at the center will be able to have their genome sequenced, interpreted and applied to their medical care.

The Precision Health Center will now house the second regional center for Geisinger's Autism & Developmental Medicine Institute. ADMI's first location and headquarters is located in Lewisburg at the Geisinger-Bucknell Autism & Developmental Medicine Center.

The center will also host the first of its semi-annual Genomics Symposia for health professionals and researchers on May 19 and 20.

Drugs and Targets

FDA Grants Orphan Designation To Reolysin for Malignant Glioma

FDA granted an Orphan Drug Designation to Reolysin for the treatment of malignant glioma.

Oncolytics Biotech Inc. applied for an ODD for pediatric high grade gliomas, however the FDA granted an ODD for the broader indication of malignant glioma in patients of all ages. In three previous brain cancer studies including gliomas, Reolysin was shown to infect a variety of brain tumors when delivered intravenously.

The FDA grants Orphan Drug Designation status to products that treat rare diseases, providing incentives to sponsors developing drugs or biologics. The FDA defines rare diseases as those affecting fewer than 200,000 people in the United States at any given time.

Paclical received market authorization in the Russian Federation by the Russian Ministry of Health, and is planned for launch in the second half of 2015.

Paclical, a novel formulation of paclitaxel based on XR-17 technology developed by Oasmia Pharmaceutical AB, was approved for treatment of epithelial ovarian cancer in combination with carboplatin. XR-17 is non-toxic and forms water soluble nanoparticles with paclitaxel.

The Russia-based company Pharmasyntez holds the distribution rights to Paclical in Russia and will be responsible for marketing the product in Russia and the CIS countries, including Armenia, Azerbaijan, Belarus, Kazakhstan, Kyrgyzstan, Moldova, Tajikistan, Ukraine, Georgia, Turkmenistan and Uzbekistan.

Celgene International II Sàrl entered into a strategic collaboration with MedImmune Limited, a wholly owned subsidiary of AstraZeneca PLC, to develop and commercialize anti-PD-L1 inhibitor MEDI4736 for hematologic malignancies.

MEDI4736 is a human monoclonal antibody directed against programmed cell death ligand 1, which helps tumors avoid detection by the immune system.

Under the terms of the agreement, Celgene will make an upfront payment of $450 million. Celgene will lead clinical development across all new clinical trials within the collaboration and be responsible for all costs associated with these trials until December 31, 2016, after which it is responsible for 75 percent of these costs.

Celgene will also be responsible for the global commercialization of approved MEDI4736 indications in hematology, and will receive royalty rates starting at 70 percent of worldwide sales from all uses in hematology. Royalty rates will decrease gradually to 50 percent over a period of four years after the first date of commercial sales. This collaboration agreement will become effective upon the expiration or termination of the applicable waiting periods under all applicable antitrust laws.

This strategic collaboration will initially focus on the development of MEDI4736 as combination therapy with Celgene's pipeline of products and other novel agents for hematologic disorders. MEDI4736 is not approved in any country for any indication.