THE CANCER LETTER

July 17, 2015 • www.cancerletter.com • Vol. 41 No. 28

CONFIDENTIAL

SOLUTIONS FOR FACULTY MORALE
AT THE UNIVERSITY OF TEXAS MD ANDERSON CANCER CENTER

DRAFT Advisory Paper presented to the University of Texas System Chancellor and the Executive Vice Chancellor for Health Affairs from the Faculty through the Executive Committee of the Faculty Senate, UT MD Anderson Cancer Center on June 14, 2015

MD Anderson Faculty White Paper Calls for Executive Pay Freeze, Elimination of "Two-Class System"

By Matthew Bin Han Ong

MD Anderson Cancer Center's faculty has asked the UT System to freeze the salaries of Ronald DePinho and members of his executive team until they reach a level of parity with faculty salaries, according to a white paper presented to UT System Chancellor Bill McRaven June 14.

The white paper—authored by the Executive Committee of the Faculty Senate and distributed confidentially to the faculty July 10—is arguably the most comprehensive representation of the faculty's cumulative dissatisfaction with DePinho and his administration's performance and handling of personnel matters over the past three years.

(Continued to page 2)

Iressa Returns to U.S. Market—Now with Companion Diagnostic

By Paul Goldberg

FDA approved Iressa (gefitinib) for patients with metastatic non-small cell lung cancer whose tumors have epidermal growth factor receptor exon 19 deletions or exon 21 (L858R) substitution mutations as detected by an FDA-approved test.

The drug is being approved concurrently with the therascreen EGFR RGQ PCR Kit as a companion diagnostic.

(Continued to page 5)

In Brief

Georgetown Lombardi and John Theurer To Form Cancer Research Consortium

GEORGETOWN LOMBARDI Comprehensive Cancer Center and **John Theurer Cancer Center**, part of Hackensack University Medical Center, developed a joint cancer research agenda as part of a multi-year plan to form a NCI-recognized cancer consortium.

(Continued to page 8)

White Paper Calls For Ending "Two-Class" Pay System

(Continued from page 1)

The draft documents, obtained by The Cancer Letter, are posted here.

In eight chapters, over 32 pages, the white paper proposes significant policy changes and shared governance initiatives, including:

• Creating oversight committees to review budgetary decisions and establishment of executive positions,

• Updating anti-retaliation and conflict resolution measures,

• Mandating transparent communication from the administration on all major institutional initiatives and business plans,

• Requiring written explanation if the president vetoes unanimous Promotion and Tenure Committee decisions, and implementing an appeals process,

• Rewarding clinical and research faculty by allowing 5 to 10 percent relief from the 40 percent salary grant support requirement as well as creating a compensation plan for faculty who have lost their ability to meet the requirement,

• Considering renewable term limits for Department Chairs and Division Heads to "curtail the possibility of abuse of power when authority increases,"

• Restoring authority to department chairs to define their own budgets, review, assign laboratory space, and hire faculty, and

• Re-establishing triennial "Upward Evaluations" as a means by which the faculty can hold departmental, division and executive leadership accountable.

In describing the "pervasive" low faculty morale at MD Anderson, the white paper states that DePinho's leadership has fostered a "two-class system" at the cancer center.

"There are few things as destructive to trust as a double standard," the Faculty Senate wrote in the first chapter, titled "TRUST." "There is a perception that the Executive Leadership demonstrates a lack of respect and appreciation for faculty hired during the previous administration, choosing to ignore the significance of their past contributions that made MDACC the number one cancer center for many years. This creates a two-class system and a demoralized faculty body.

"There is also a perception that the new recruits have been provided or promised excessive resources in terms of salary support, research funds, and leadership of programs."

The authors go on to describe how new recruits are paid twice as high as existing faculty.

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.

This communication between the faculty and the UT System is a good thing, MD Anderson officials said July 13 in a statement to The Cancer Letter.

"The University of Texas MD Anderson Cancer Center respects the private communication between the UT System Chancellor and MD Anderson's Faculty Senate Leadership, and encourages a continued and open exchange of ideas and opinions," officials said. "Candid dialogue is fundamental to building trust and finding resolution."

In February, the Faculty Senate passed a resolution

Editor & Publisher: Paul Goldberg
Associate Editor: Conor Hale
Reporter: Matthew Bin Han Ong
Interns: Nick Crispino

Editorial, Subscriptions and Customer Service:
202-362-1809 Fax: 202-379-1787
PO Box 9905, Washington DC 20016
General Information: www.cancerletter.com

Subscription $405 per year worldwide. ISSN 0096-3917. Published 46 times a year by The Cancer Letter Inc.

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)

asking UT System officials and the Board of Regents to "provide guidance" to DePinho's administration "in establishing milestones and timelines to implement measures to improve the morale of the faculty and the general health of the Institution." (The Cancer Letter, Feb. 17)

UT System Chancellor Bill McRaven responded March 18, asking the Faculty Senate to draft a white paper. In that closed-door meeting, McRaven said that he had laid out "some clear guidance" for DePinho (The Cancer Letter, March 20).

"I have talked to Ron about how we improve the shared governance," McRaven said to the faculty March 18. "Your voice should be not only heard, but it should be understood. It should be looked at in the context of what's going on here at MD Anderson every single step of the way. And I believe that firmly."

The support of the UT System for MD Anderson and its leadership has been "strong and unwavering," McRaven said in a statement July 13 to The Cancer Letter.

"MD Anderson is a crown jewel of the UT System because of its international recognition for the excellence of its patient care and the groundbreaking contributions of its researchers and scientists," McRaven said. "This institution has been built through the hard work and dedication of its faculty, staff and administration.

"In every meeting that I have had with representatives of the institution, their passion and dedication is nothing short of inspirational. As a leader in the field, however, MD Anderson must constantly look to the future to be even better and more effective.

"It is in that spirit that I have solicited thoughts and suggestions from the Faculty Senate, the Division Directors and the executive leadership team.

"The prioritized areas of opportunity for improvement are remarkably consistent across these groups, and soon I will be communicating to all of them my suggestions for shared work on these initiatives."

McRaven: "Not Afraid of Self-Criticism"

McRaven said his idea for the white paper is rooted in his military experience.

"During my time in the military, the SEAL Teams were known for being one of the best organizations in the service," McRaven wrote to The Cancer Letter. "The reason we were so good was our willingness to aggressively critique our training and real world missions so that we got better each time we launched.

"These After Action Reviews (AARs) were blunt, sometimes scathing and oblivious to personal sensitivities. They included every member of the SEAL Team from the most junior SEAL to the Commanding Officer. Everyone had an equal voice in the AAR and no one was penalized for their comments. It was the only way we could improve, and the lives of my men depended on improving every day.

"It was with this idea in mind that I asked the MD Anderson faculty to develop a White Paper that, from their point of view, identified problem areas and opportunities for improvement. I asked for a broad representation of the faculty and encouraged candor. The faculty provided me a long version that was quite detailed and somewhat tactical.

"Consequently, I requested a more tailored approach to address the big issues. President DePinho and the leadership of MD Anderson wholeheartedly supported this approach, and I am incredibly proud of them for their willingness to hear and address some of the uncomfortable and complex problems that need to be worked out.

"The White Paper is treated as draft input to me, the Chancellor. I will make the decision on how best to use this information and how to engage the MD Anderson leadership on steps for continuous improvement of the institution. We are convening a team from the MD Anderson Executive Committee of the Faculty Senate, the Division Heads and the Senior Leadership to help me review the input and provide appropriate counsel to President DePinho and others.

"The best organizations in the world must constantly assess their progress. The best organizations in the world are not afraid of self-criticism. They embrace it knowing they will be stronger in the long run.

"Whether you are internal to MD Anderson or are observing from the outside, this is exactly what you should expect your leaders to do. Anything less should be unacceptable. It is what will continue to make MD Anderson the best Cancer Center in the world.

"I am profoundly grateful to the entire MD Anderson faculty community, including its Senate and faculty-at-large, and to President DePinho and executive leadership team for focusing on what matters most—doing everything in their power, both individually and collectively, to ensure that MD Anderson's patients will be benefit from all that this extraordinary institution has to offer them."

The full text of the Executive Committee of the Faculty Senate email to MD Anderson faculty follows:

The Executive Committee of the Faculty Senate request that all the attached materials and this email be kept absolutely confidential and not be forwarded to anyone.

Dear Faculty:

In the interest of transparency, we would like to share with you the process used to create the attached *draft documents created as advisory to the Chancellor*. Throughout this process we realized we would not be able to get 100% consensus on all topics, and some items may not fully represent the opinion of each of our more than 1,600 faculty members.

Initially, we received a charge from the Chancellor to come up with a draft advisory white paper outlining the issues that resulted in the low faculty morale, which has been pervasive throughout the institution the last few years.

Using the Faculty Senate, institutional, and UT System surveys, as well as information obtained during formal visits of the Senate leadership to individual Departments we began the process to create a first draft.

Additionally, we solicited faculty feedback which was provided to us through (1) the Division Heads who provided each division's full reports assembled from departmental faculty suggestions gathered in response to the leadership's post-UT Survey question of "what are the top issues/solutions that can improve faculty morale?" and (2) direct communications to the Senate office from faculty at large in response to emails requesting this information.

We sent an early draft white paper first to the Division Heads for feedback. The Divisions Heads suggested an Executive Summary of the issues, which we drafted and then distributed to the faculty through the Division Heads and the Chairs.

The draft was then revised with the additional feedback we received from you. The full document was also made available for faculty viewing in the Faculty Senate office from which we gathered additional feedback. The attached documents are the current work in progress.

These documents were created as *draft advisory documents to Chancellor McRaven*, providing a broad view of the issues from the faculty relating to low faculty morale. The draft documents are now in the Chancellor's hands, and he and Executive Vice Chancellor Greenberg will determine future directions and plans related to these advisory documents.

We would like to thank the Division Heads and Department Chairs for partnering with us throughout this process. We would also like to extend a special thank you to the many faculty members for taking the time to provide valuable feedback to the Chancellor and the Executive Vice Chancellor.

Your input will help the Chancellor and the Executive Vice Chancellor to make informed decisions that will improve the morale at MD Anderson. Thank you for your participation.

- Executive Committee of the Faculty Senate

Iressa Returns to U.S. Market With Companion Diagnostic

(Continued from page 1)

Iressa is sponsored by AstraZeneca and therascreen by QIAGEN N.V.

In the U.S., therascreen has been marketed since 2013 as a companion diagnostic for the Boehringer-Ingelheim agent Gilotrif (afatinib).

Iressa is now approved for the same indication as Gilotrif.

Iressa's July 13 approval is the case of science catching up with the drug. Iressa, the first EGFR inhibitor to get on the market, first received an accelerated approval in 2003, but was placed in a restricted access program two years later, after a confirmatory trial failed to demonstrate a survival advantage.

Iressa was first approved for third-line NSCLC, without differentiation for any specific mutation—since at that time it was unknown whether the existence of the mutation predicted a response (The Cancer Letter, May 9, 2002). And, of course, there was no diagnostic.

The drug squeaked through the approval process with an accelerated approval based on data from phase II trials showing 13.6 percent of U.S. patients achieved tumor shrinkage of at least 50 percent, after their disease had progressed, following failure of both platinum-based and docetaxel chemotherapies. The accelerated approval was granted in spite of negative randomized trial.

The FDA Oncologic Drugs Advisory Committee was evidently influenced by testimony of a large number of patients who said they benefited from treatment (The Cancer Letter, Sept. 27, 2002). At the time, these outcomes couldn't be fully explained.

The fact that these patients clearly experienced a benefit clearly surprised ODAC members. However, the reason for this benefit—or the definition of the population that experienced the benefit—was unknown at the time (The Cancer Letter, Nov. 8, 2002). While scientists believed that the drug was hitting a target, there was no way to preselect patients who would be candidates for getting Iressa.

A confirmatory randomized trial powered to detect survival came up negative, causing great disappointment and cessation of further clinical investigations by clinical trials cooperative groups (The Cancer Letter, Jan. 7, 2005; Jan. 29, 2005; April 22, 2005).

Meanwhile, the data for a similar agent, Genentech's Tarceva (gefitinib), was positive for extending survival, and the drug was approved for second-line indication in November 2004. This two-month survival advantage (6.7 months for Tarceva vs 4.7 for placebo) was visible even without limiting the population to patients with specifying the population.

As a result, in 2005, FDA placed Iressa in a limited access program (The Cancer Letter, June 24, 2005). The drug was to be available only to patients who were at the time responding to the therapy or had responded to it in the past. All others were to be switched to Tarceva.

The science that would ultimately explain response to Iressa and Tarceva started to emerge in the midst of the Iressa controversy (The Cancer Letter, May 6, 2005).

Methodology for determining response to the drug is covered by U.S. patent #7294468, which has the priority date of March 31, 2004 and a publication date of Nov. 13, 2007. The technology was invented at Dana-Farber Cancer Institute and Massachusetts General Hospital.

Though the drug was almost completely withdrawn in the U.S., Iressa remained on the market in about 70 countries.

In Europe, the drug's indication was expanded to all lines of therapy of metastatic or locally advanced NSCLC with activating mutations in 2009 (The Cancer Letter, July 31, 2009). The European approval of Iressa was based on two non-inferiority trials.

• One trial, called INTEREST, compared Iressa with Taxotere (docetaxel) as second-line treatment for NSCLC.

• The other, IPASS, compared Iressa with carboplatin and paclitaxel as a front-line therapy in a cohort enriched with groups that are known to respond to this class of drugs: Asians, non-smokers, and patients with adenocarcinoma. Also, 79 percent of patients enrolled were women, another group believed likely to have a better response to Iressa.

Iressa's current U.S. prescribing information is available through the FDA's website.

A list of all companion diagnostics approved by FDA is posted here.

FDA's summary of the data follows:

The approval of gefitinib was based on the results of a multicenter, single-arm, open-label clinical study of a total of 106 treatment naive-patients with metastatic EGFR mutation positive NSCLC who received gefitinib at a dose of 250 mg daily until disease progression or intolerable toxicity.

The major efficacy outcome was objective response rate according to RECIST v1.1 as evaluated by both a Blinded Independent Central Review and investigators. The BICR ORR was 50 percent (95%

CI: 41, 59) with a median duration of response of 6.0 months. Investigator-determined ORR was 70 percent (95% CI: 61, 78) with a median DoR of 8.3 months.

Efficacy results were supported by an exploratory analysis of a subset of a randomized, multicenter, open-label trial conducted in patients with metastatic adenocarcinoma histology NSCLC receiving first-line treatment. Patients were randomized (1:1) to receive gefitinib 250 mg once daily or up to 6 cycles of carboplatin/paclitaxel.

The efficacy outcomes included progression-free survival and ORR as assessed by the BICR. The subset population consisted of 186 of 1217 patients (15 percent) determined to be EGFR positive and had radiographic scans available for a retrospective assessment by a BICR. In this subset, there were 88 gefitinib-treated patients and 98 carboplatin/paclitaxel-treated patients.

The hazard ratio for PFS in the gefitinib-treated arm was 0.54 (95% CI: 0.38, 0.79) with a median PFS of 10.9 months for the gefitinib-treated patients and 7.4 months for the carboplatin/paclitaxel-treated patients as assessed by BICR. In addition, the BICR ORR was 67 percent (95% CI: 56, 77) with a DoR of 9.6 months for gefitinib-treated patients and 41 percent (95% CI: 31, 51) with a DoR of 5.5 months for carboplatin/paclitaxel-treated patients.

Safety data was evaluated for common adverse reactions in a double-blind placebo- controlled trial of 1692 patients. Of the 1,129 patients who received gefitinib, the most common (greater than or equal to 20 percent) adverse reactions in order of decreasing frequency were skin reactions, aspartate aminotransferase increased, alanine aminotransferase increased, proteinuria, and diarrhea. The most common (greater than or equal to 2 percent) grade 3-4 adverse reactions were proteinuria, diarrhea, ALT increased, decreased appetite, AST increased, and skin reactions. Approximately 5 percent of gefitinib-treated patients discontinued treatment due to an adverse reaction.

Serious and uncommon adverse drug reactions were evaluated in 2462 patients with NSCLC who received gefitinib monotherapy in three randomized clinical studies. Significant adverse reactions were interstitial lung disease, which occurred in 1.3 percent of patients, fatal hepatotoxicity which occurred in 0.04 percent of patients, and grade 3 ocular disorders which occurred in 0.1 percent of patients.

Follow us on Twitter: @TheCancerLetter

Letter to the Editor

NCCS: Covering End-of-Life Planning is a Step Toward Delivering Patient-Centered Care

By Shelley Fuld Nasso

Last week, the Centers for Medicare & Medicaid Services announced plans to support Medicare beneficiaries by reimbursing doctors for advance care planning beginning in January 2016.

The proposed codes would reimburse for discussions about an individual's wishes, should he or she becomes too ill to make decisions, and for the completion of an advance directive.

We believe CMS' proposal to reimburse for advance care planning is an important step toward providing patient-centered care that respects people's wishes at the end of their lives. We know there is a disconnect between how people die—often in the hospital with aggressive treatment—and what people most often report they want at the end of life—to die at home, surrounded by loved ones.

One reason is the failure to have difficult discussions about values and preferences for care at the end of life. There are a number of reasons these discussions don't happen, one of which is that the discussions can be lengthy, and physicians do not have enough time under the current reimbursement mechanisms.

Medicare's new payment proposal is an incentive for providers to have these important conversations in a compassionate and patient-centered way.

The advance care planning code is one of several services CMS has proposed in recent years to reimburse for important cognitive services that are essential to improving the quality of care patients receive. Previous proposals include transitional care management code, for managing discharge from the hospital or other qualified setting, and a chronic care management code, for non-face-to-face care management for certain beneficiaries. These codes are important but not sufficient to meet the needs of cancer survivors.

This is why the National Coalition for Cancer Survivorship has long advocated for cancer care planning, at diagnosis and at major transition points during treatment and survivorship. The recently introduced Planning Actively for Cancer Treatment Act (H.R. 2846) would create a Medicare service for cancer care planning.

The planning service could be provided to patients

at the time of cancer diagnosis, at the end of active treatment and beginning of long-term survivorship, and when there is a significant change in treatment. The cancer care planning process will produce a written plan of care provided to the patient for use in managing care.

The PACT Act would provide reimbursement for this service, which is important to patients but is not standard practice because current reimbursement mechanisms do not support the time required by physicians and the care team to complete a thorough cancer care planning process.

Cancer care planning is distinct from advance care planning, and in our view, many cancer patients, particularly those with advanced or metastatic cancer, need both services as part of their care. Cancer care planning needs to happen early, beginning at diagnosis, and should include a discussion of the intent of treatment. A truly patient-centered treatment planning discussion prepares the way for a more productive advance care planning experience.

Both advance care planning and cancer care planning require patient involvement in the decision-making about their care. These discussions can be difficult, and both physicians and patients need help to have those conversations.

There are efforts to train physicians to have meaningful conversations with patients. NCCS has developed tools to help prepare patients to be engaged in decisions about their care and to express their values and preferences. We also encourage patients to assert themselves in requesting cancer care planning and shared decision-making.

The PACT Act is supported by:

American Society for Clinical Oncology
American Cancer Society Cancer Action Network
CancerCare
C-Change
Fight Colorectal Cancer
International Myeloma Foundation
Kidney Cancer Association
The Leukemia & Lymphoma Society
The LIVESTRONG Foundation
Lymphoma Research Foundation
National Coalition for Cancer Survivorship
National Comprehensive Cancer Network
National Patient Advocate Foundation
Ovarian Cancer National Alliance
Prevent Cancer Foundation
Susan G. Komen
The University of Arizona Cancer Center
University of Kansas Cancer Center
Comprehensive Cancer Center of Wake Forest University
Lombardi Comprehensive Cancer Center at Georgetown University

The author is chief executive officer of the National Coalition for Cancer Survivorship.

Funding Opportunity

DoD Taking Applications for $75,000 Horizon Grant

The Department of Defense is taking applications for its Horizon Award, which offers up to $75,000 in funding to support junior-level scientists to conduct impactful research with the mentorship of an experienced cancer researcher.

The award is for principal investigators, both pre-doctoral candidates and postdoctoral fellows are eligible, and mentors that have a strong record of funding and publications. The PI and mentor must be from the same organization.

They must address at least one of the congressionally directed FY15 PRCRP Topic Areas and are encouraged to address at least one of the FY15 PRCRP Military Relevance Focus Areas. Research applications in the areas of breast, prostate, lung (excluding mesothelioma), or ovarian cancer will not be accepted.

The FY15 PRCRP Topic Areas are: cancers of the kidney, liver, pancreas, stomach or colorectal tract; melanoma and other skin cancers; myeloproliferative disorders; listeria vaccines for cancer; mesothelioma; and neuroblastoma. Liver and stomach cancer have been newly added for 2015.

The FY15 Military Relevance Focus Areas are: Militarily relevant risk factors associated with cancer (e.g., ionizing radiation, chemicals, infectious agents, and environmental carcinogens); and gaps in cancer prevention, screening, early detection, diagnosis, treatment, and/or survivorship that may affect the general population but have a particularly profound impact on the health and well-being of military members, veterans, and their beneficiaries.

Full applications are due Aug. 11. Clinical trials are not allowed and preliminary data are not required. The maximum period of performance is one year.

A pre-application is required through the electronic Biomedical Research Application Portal at http://eBRAP.org prior to the pre-application deadline.

Program announcements and general application instructions are available at www.grants.gov.

In Brief

Georgetown Lombardi and John Theurer to Form Cancer Research Consortium

(Continued from page 1)

Georgetown Lombardi is an NCI-designated comprehensive cancer center. Through the partnership, John Theurer Cancer Center is working to secure this NCI designation as well.

Among the planned joint research projects is blood stem cell transplantation and immunotherapy clinical research at Washington DC's Blood and Marrow Stem Cell Transplant Program, established in 2013 by John Theurer and MedStar Georgetown University Hospital, Georgetown Lombardi's clinical partner.

The research areas include expansion of clinical bone marrow transplant research; clinical study of haplo transplants, the use of half-matched stem cell donor cells; re-engineering the function and focus of key immune cells; and the investigation of immune checkpoint blocking antibodies.

Next generation genomic sequencing research will utilize the Clinical Outcomes Tracking & Analysis Platform, a large cancer patient treatment and outcomes database developed by John Theurer Cancer Center to sort patients and reduce variance.

The two organizations will also explore population science research and expand existing programs focused on the characteristics of patients in the greater Washington and the northern New Jersey areas. The John Theurer Cancer Center will establish a Cancer Prevention and Control office and Georgetown Lombardi will expand its population science research using the COTA database platform.

CITY OF HOPE established an endowed professorship with a $1.5 million gift from the **Norman and Sadie Lee Foundation**. The professorship will be used to advance research, education and clinical activities in support of head and neck cancer treatment.

The first professorship will be awarded to **Ellie Maghami**, chief of head and neck surgery at City of Hope.

As the holder of The Norman and Sadie Lee Professorship in Head and Neck Cancer, Maghami will further develop therapies with an emphasis on molecular targets to make head and neck cancers more sensitive to therapy.

Philanthropist Norman Lee served on the City of Hope board of directors from 1985 to 1987. The Lees also were instrumental in the visit by the Queen of England to the City of Hope campus in 1983 for the official dedication of the Sadie and Norman Lee British Pediatric Research Center on the Duarte campus.

Maghami has already developed a retroviral gene therapy targeting a novel cancer gene that is overactive in nearly half of head and neck cancers of the mucous membranes. She has authored more than 21 peer-reviewed publications and has won numerous awards, including the 2004 ASCO Young Investigator Award. She is councilor-at-large for the American Head and Neck Society and also serves on the National Comprehensive Cancer Network Committee on Head and Neck Cancer.

MARYANN ROEFARO was named co-chair of the **Community Oncology Alliance Administrators' Network**.

Roefaro, CEO of Hematology-Oncology Associates of Central New York, joins **Kim Woofter**, who is currently serving as a CAN co-chair. Woofter serves as COO of Michiana Hematology Oncology.

The network, established in 2008, has over 300 members from community oncology practices across the U.S. Roefaro and Woofter are both longtime network members, according to COA.

The network recently hosted a series of four web conferences about the Center for Medicare and Medicaid Innovation Oncology Care Model applications. CMMI is developing a new payment and delivery model.

SYNEXUS opened three dedicated research centers in Bulgaria, Poland and Romania, bringing the total to nine centers in Eastern Europe and a total network of 25 across Europe and Africa.

Synexus, based in the U.K., is a multi-national company focused on the recruitment and running of clinical trials.

The Polish facility in Gdansk is Synexus' largest research center. Magdalena Przekwas-Jaruchowska, the center's director, oversaw the opening ceremony which included representatives from the local authority, the British Embassy, the medical university and patients' associations.

Romania's center is based in the capital, Bucharest, which has a population of two million. The dedicated research center in Bulgaria is situated in Sofia, and aims to offer access to treatments in pulmonology, rheumatology, neurology, endochrinology, cardiology, gastroenterology and dermatology.

ACT for NIH added seven members to its advisory committee.

They are: **Retta Beery**, founder of Hope Knows No Boundaries; **Former Rep. Eric Cantor**, currently vice chairman and managing director of investment bank Moelis & Company; **Former Sen. Tom Harkin**, now of The Harkin Institute for Public Policy and Citizen Engagement; **Siddhartha Mukherjee**, author of Emperor of All Maladies: A Biography of Cancer; **Perry Nisen**, CEO of Sanford Burnham Prebys Medical Discovery Institute; **Sean Parker**, founder of The Parker Foundation; and **Lori Wilson**, associate professor of surgery at the Howard University College of Medicine.

These members join the current advisory committee, which includes: David Baltimore, president emeritus of the California Institute of Technology; Ronald DePinho, president of MD Anderson Cancer Center; Jennifer Doudna, professor at the University of California, Berkeley; Bernadette Gray-Little, chancellor of the University of Kansas;Michael Milken, public health advocate; and Ronald Petersen, director of Mayo Alzheimer's Disease Research Center and professor of Neurology Mayo Clinic College of Medicine.

Drugs and Targets

EU Approves Imbruvica in WM

The European Commission approved Imbruvica capsules (ibrutinib) for adult patients with Waldenstrom's macroglobulinemia who have received at least one prior therapy, or in first line treatment for patients unsuitable for chemo-immunotherapy.

Imbruvica is co-developed by Cilag GmbH International, a member of the Janssen Pharmaceutical Companies, and Pharmacyclics LLC, an AbbVie company. Janssen affiliates market ibrutinib in Europe, the Middle East and Africa, as well as the rest of the world, except for the U.S., where it is co-marketed by Janssen Biotech Inc. and Pharmacyclics.

Imbruvica has already been approved in Europe for the treatment of adult patients with relapsed or refractory mantle cell lymphoma, or adult patients with chronic lymphocytic leukemia who have received at least one prior therapy, or in first line in the presence of 17p deletion or TP53 mutation in patients unsuitable for chemo-immunotherapy. Imbruvica has also been recently approved for the treatment of WM by the U.S. FDA, which granted it Breakthrough Therapy Designation in 2013.

Genome sequencing of patients with WM has revealed a common mutation in the MYD88 gene. This mutation triggers the activation of a number of targets, including Bruton's tyrosine kinase, which is a key component needed to regulate immune cell proliferation and cell survival which plays a part in B-cell malignancies, such as WM. Imbruvica forms a strong covalent bond with BTK, thereby inhibiting the enzyme and blocking the transmission of cell survival signals within the malignant B cells.

The phase II multi-center study on which the approval was based evaluated the efficacy and tolerability of Imbruvica 420 mg once daily in 63 patients with previously treated WM (median age of 63; range, 44-86 years old).

Updated results from the study were published in April in The New England Journal of Medicine. The overall response rate using criteria adopted from the International Workshop on WM was 90.5 percent, 57 out of 63 patients (95 percent CI 80.4-96.4).

Eleven patients (17 percent) achieved a minor response, 36 patients (57 percent) achieved a partial response (PR) and 10 patients (16 percent) achieved a very good PR. The median times to at least minor and partial responses were four weeks and eight weeks respectively.

Secondary endpoints of the registration trial included progression free survival and the safety and tolerability of Imbruvica in symptomatic patients with previously treated WM. The estimated two-year PFS and overall survival rates among all patients were 69.1 percent (95% CI 53.2-80.5) and 95.2 percent (95% CI 86.0-98.4) respectively.

FDA granted an Orphan Drug Designation to ImMucin for the treatment of multiple myeloma, developed by Vaxil Bio.

ImMucin trains the patient's immune system to identify and destroy cells which display a short specific 21-mer portion (signal peptide domain) of the cancer-associated expression of MUC1, which appears on 90% of all cancer cells but not in patient blood.

Vaxil completed a phase I/II clinical study with ImMucin in MM patients, which showed strong diversified T/B-cell immunity in all 15 patients across MHC repertoires and initial indications of clinical efficacy; 11 out of the 15 treated patients demonstrated stable disease or clinical improvement which did not require any further treatment.

An ongoing follow-up study in patients who responded clinically to ImMucin has shown that some patients haven't required any further treatment for their disease in the four years since ImMucin treatment.

FDA granted an Orphan Drug Designation to Cleave Biosciences' lead drug candidate, CB-5083, for treatment of multiple myeloma.

CB-5083 is a first-in-class, oral inhibitor of p97, an enzyme that controls various aspects of protein homeostasis.

Cleave's ongoing studies include an open-label, phase I dose escalation/dose expansion trial to evaluate the safety, pharmacokinetics, pharmacodynamics and anti-tumor activity of CB-5083 in multiple myeloma patients who have relapsed/refractory or refractory disease after receiving two or more lines of therapy, including an immunomodulatory agent and a proteasome inhibitor.

Cleave expects to enroll up to 60 patients at multiple U.S. cancer centers that are part of the Multiple Myeloma Research Consortium. A second phase I study of CB-5083 is focused in patients with solid tumor malignancies.

FDA granted Fast Track designation to immuno-oncology products Toca 511 and Toca FC, developed by Tocagen Inc., for the treatment of recurrent high grade glioma, including glioblastoma and anaplastic astrocytoma. A study in this indication is planned for later this year, according to Tocagen.

Toca 511 and Toca FC are designed to selectively transform cancer cells so they produce a chemotherapy drug within the tumor while also activating the immune system against the tumor with local and systemic benefits.

Toca 511 is a retroviral replicating vector that selectively delivers a gene for the enzyme cytosine deaminase to the cancer cells. The patient then takes oral cycles of Toca FC, a novel formulation of an antifungal drug, which is converted into the FDA-approved chemotherapy drug, 5-fluorouracil.

FDA granted priority review to MM-398 in patients with metastatic adenocarcinoma of the pancreas who have been previously treated with gemcitabine-based therapy.

The goal is for the FDA to take action on the marketing application within six months of receipt (compared with 10 months under standard review) of the NDA submission.

MM-398 (PEP02, irinotecan liposome injection), also known as "nal-IRI," is a novel, stable nanotherapeutic encapsulation of the marketed chemotherapy drug irinotecan.

In May 2011, PharmaEngine Inc. and Merrimack Pharmaceuticals executed an exclusive license agreement. Under the terms of the agreement, PharmaEngine granted back Merrimack the rights to develop, manufacture, and commercialize PEP02 (designated as MM-398 by Merrimack) in Asia and Europe, and retained the same rights in Taiwan. In September 2014, Merrimack licensed the rights to MM-398 outside of the U.S. and Taiwan to Baxter International's BioScience business.

In 2011, MM-398 received orphan drug designation from both the FDA and the EMA for the treatment of pancreatic cancer.

Eli Lilly and Co. and Immunocore Ltd. entered into an immunotherapy-based clinical trial collaboration to explore the utility of Immunocore's lead T cell receptor-based investigational therapeutic, IMCgp100, in combination with Lilly's galunisertib (LY2157299) and merestinib (LY2801653).

The goal of the collaboration is to identify combination regimens effective in patients with metastatic cutaneous and uveal melanomas.

Under the terms of the agreement, Immunocore and Lilly will conduct a phase Ib/II clinical study evaluating the safety and preliminary efficacy of IMCgp100 in combination with galunisertib in metastatic cutaneous melanoma.

A second phase Ib/II study will be conducted combining IMCgp100 with merestinib in metastatic uveal melanoma. Lilly will act as trial sponsor. These studies are anticipated to begin in 2016. No financial terms were disclosed.

IMCgp100 is an immune mobilizing mTCR Against Cancer molecule—or ImmTAC, a novel class of bi-specific biologic drugs based on T cell receptors with an affinity for intracellular and extracellular cancer targets.

Lilly's galunisertib is a small molecule inhibitor of TGF beta R1 kinase that in vitro selectively blocks TGF beta signaling. TGF beta promotes tumor growth, suppresses the immune system and increases the ability of tumors to spread in the body. Merestinib is Lilly's small molecule multi-kinase inhibitor that in vitro selectively blocks signaling of MET, MST1R (RON), AXL, and MKNK1/2, pathways that potentially play a role in metastatic uveal melanoma.

This is Immunocore and Lilly's second collaboration. The companies entered into a co-discovery and co-development collaboration in July 2014 to research other novel T cell-based cancer therapies built on Immunocore's ImmTAC platform.