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DISSENTERS IN ANTI-TOBACCO MOVEMENT CITE NATIONAL ACADEMY REPORT IN CLAIM THAT "E-CIGARETTES ARE SAVING LIVES." NOPE, THE NAS REPORT'S AUTHORS SAY

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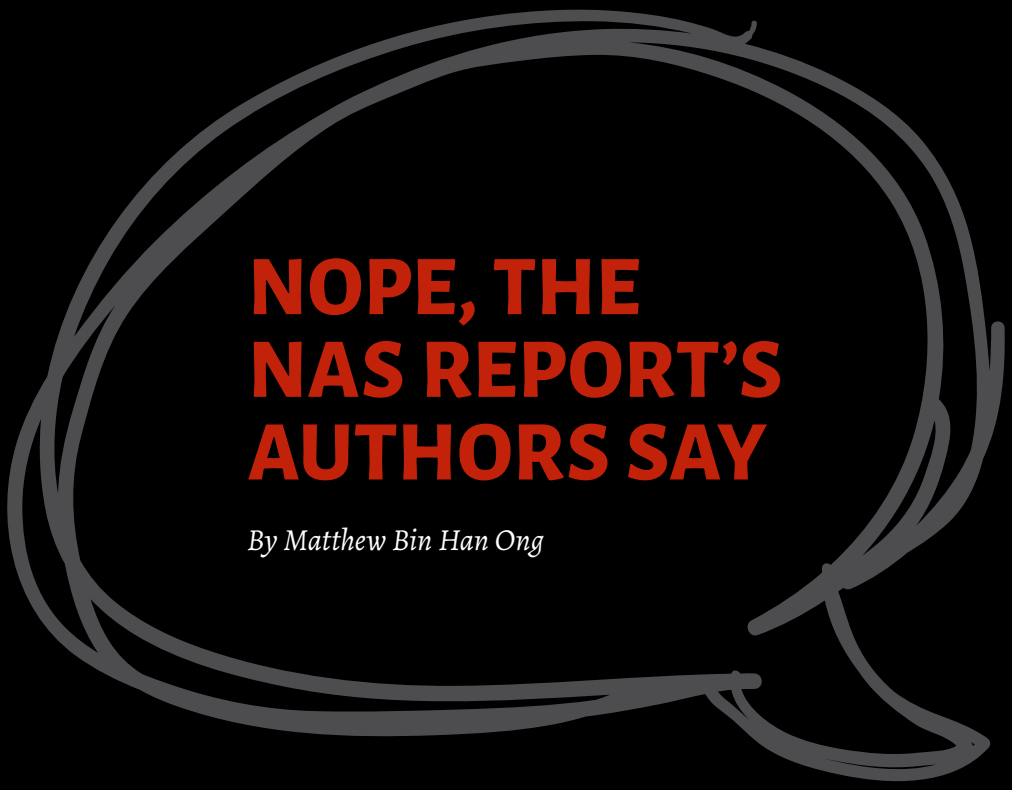

NOPE, THE NAS REPORT'S AUTHORS SAY

By Matthew Bin Han Ong

A group of tobacco control advocates, one of whom receives money from Philip Morris International, issued a press release trumpeting that "E-Cigarettes are Saving Lives," and attributed this conclusion to a recent report by the National Academy of Sciences, Engineering, and Medicine.

The authors of the FDA-commissioned NASEM report, titled "Public Health Consequences of E-Cigarettes" say they wrote nothing of the sort, and mainstream leaders in the anti-tobacco world say the statement is a clear misrepresentation of the NASEM report.

The inflated claims were made by the National Tobacco Reform Initiative, an advocacy group focused on reducing "the number of adult smokers in the U.S. by at least 15 million by the year 2024, an interagency-approved goal."

The group, called NTRI, includes Derek Yach, founder of the Foundation for a Smoke-Free World, an organization which has received a pledge for $1 billion in "cancer research" funds from Philip Morris International (The Cancer Letter, Oct. 6, 2017).

John Seffrin, former CEO of the American Cancer Society, who is now a professor of practice at Indiana University Bloomington School of Public Health is a supporter of Yach's initiative and a contact on the NTRI press release about the NASEM report.

Tobacco companies like Philip Morris are losing customers of products that involve burning tobacco and are increasingly emerging as dominant players in the market for alternative products, which involve electronic cigarettes and similar devices. Meanwhile, mainstream tobacco control organizations say that while alternative products may present a safer alternatives, their prevalence and harms must be studied.

One of the key concerns is dual use, a situation where consumers use both conventional cigarettes and e-cigarettes.

The NASEM study did just that, summarizing available evidence, presenting it in a nuanced way, and—of course—making no bombastic claims. NTRI, run by an seven-member "core team" that includes Yach and Seffrin, urged news organizations to "publish the attached Press Release related to harm reduction." The text of the press release appears on page 6.

The NTRI statement was accompanied by endorsements from—according to the email—three "top national public health leaders," including Seffrin and David Abrams, professor, Department of Social and Behavioral Sciences at the New York University College of Global Public Health, as well as Allan Erickson, former national vice president for public education at the American Cancer Society.

A quick look at NTRI's "About Us" page shows that Seffrin, Abrams, and Erickson are part of the group's "Core Team for Tobacco Control." Yach, a former official at World Health Organization who now runs a Philip Morris-funded research foundation, was not listed as a contact on the press release.

"None of us are on the foundation other than Derek Yach," NYU's Abrams said to The Cancer Letter. "He is a member of our group and as an individual has input in what we do. I think actually, Derek may be the only member that's currently associated with the foundation. There's no one else that I'm aware of in NTRI that has any affiliation with that foundation.

In the NTRI statement, Seffrin says that "after fighting the tobacco epidemic for over five decades, we now have proven harm reduction methods to help us avoid a carnage in otherwise preventable deaths."

Seffrin's current stance puzzles many of his former colleagues at ACS and the mainstream anti-tobacco movement in part because during his tenure at the society Seffrin had engineered one of the most stringent conflict policies on tobacco funding.

Today, anyone who does business with ACS—as a funded researcher or a contractor—continues to be precluded from taking money from sources tainted by tobacco. Tough conflict of interest rules are needed because tobacco companies have historically sought to create appearances of scientific debates over safety of their products, mainstream advocates say. A situation where "experts disagree" disarms anti-tobacco campaigns, postpones regulatory actions, and allows tobacco companies to keep selling products.

The NASEM report does not say, "e-cigarettes are saving lives," David Eaton, chair of the NASEM committee that authored the report, said to The Cancer Letter.

"It is understandable how someone might interpret the modeling results as saying that 'e-cigarettes saves lives,' but this is not what our report stated," said Eaton, dean and vice provost of the Graduate School at the University of Washington, Seattle. "The modeling, of course, is exactly that, and is totally dependent on the validity of the assumptions that go into the model, which are uncertain with our current state of knowledge.

"While one might conclude from our report that a smoker who switches to e-cigarettes has reduced his/her risk, there is some uncertainty, and the evidence suggests that they must switch COMPLETELY (e.g., reduced risk from 'dual use' is uncertain)."

The full text of Eaton's statement appears on page 7.

NTRI's interpretation of NASEM's findings is irresponsible, said Stanton Glantz, director of the Center for Tobacco Research Control & Education at the University of California San Francisco.

"The statement misrepresents the conclusions in the NAS report about e-cigs and their effect on smokers' quitting," Glantz said to The Cancer Letter. "The actual report is ambivalent on this point, noting that the studies are mixed. The NAS report does say that

switching completely to e-cigs would be less risky, a point most people (including me) agree with, but the reality is that complete switching is rare. Most e-cig users are dual users."

The full text of Glantz's statement appears on page 9.

NTRI is overstating the NASEM report findings, said Matthew Myers, president of Campaign for Tobacco-Free Kids.

"In fact, the chair of the committee that wrote the report stated that, based on the current evidence, 'E-cigarettes cannot be simply categorized as either beneficial or harmful,'" Myers said to The Cancer Letter. "The report does not say and cannot reasonably be interpreted to say that there is sufficient evidence to recommend that smokers switch to e-cigarettes as a primary mitigation strategy."

be less risk associated with their use compared to conventional cigarettes. It is difficult to adopt a relative risk strategy for e-cigarettes when there isn't any evidence evaluating their long-term health effects."

The full text of Bhatnagar's statement appears on page 11.

FDA officials declined to comment on NTRI's recommendations and instead pointed to the agency's plan to lower nicotine in cigarettes to non-addictive levels. Specifically:

"The FDA plans to begin a public dialogue about lowering nicotine levels in combustible cigarettes to non-addictive levels through achievable product standards," agency officials wrote in a July 2017 news release. "The agency intends to issue an Advance Notice of Proposed Rulemaking (ANPRM) to seek input on the potential public health benefits and any possible adverse effects of lowering nicotine in cigarettes."

Cancer Letter. "They have considerable potential to help smokers who cannot or will not otherwise quit using nicotine, thereby potentially producing a net public health benefit.

"But to accomplish that end, much work lies ahead—significant, effective public education and guidance to clinicians—and this must be managed in a responsible manner to avoid unintended consequences."

The full text of Drope's statement appears on page 8.

Sources close to NASEM said they would caution against promotion of e-cigarettes. While the NTRI press release was largely consistent with the NASEM report, insiders said, NTRI ignored the downside evidence that e-cigarettes may introduce teens and young adults to begin smoking cigarettes.

The "abundance of caution" slows the ability to save lives, said NYU's Abrams, a member of the NTRI's core team.

"Ideology and prior old-school thinking can color and distort the current reality, because some people are ultimately embracing the precautionary principle, and what that is, is when we have doubts, therefore, we should be very conservative and we cannot support e-cigarettes," said Abrams, a former member of the NCI Board of Scientific Advisors and former director of the NIH Office of Behavioral and Social Sciences Research. "It came out of, I think, the very correct view that when death and disease are very, very high, there's an urgency to think about the precautionary principle a little differently.

"When a disease is killing people quickly and you have inadequate alternatives, you're better off allowing some risks of a new product in order to save lives."

A conversation with Abrams appears on page 13.

> It is understandable how someone might interpret the modeling results as saying that 'e-cigarettes saves lives,' but this is not what our report stated.
>
> *– David Eaton*

The full text of Myers's statement appears on page 10.

NTRI's interpretation of the NASEM report is inaccurate, said Aruni Bhatnagar, professor of medicine, director of the Diabetes and Obesity Center at the University of Louisville, and fellow of the American Heart Association.

"The NASEM report did not indicate or suggest that e-cigarettes are saving lives," Bhatnagar said to The Cancer Letter. "It said that because there are fewer toxins in e-cigarettes, there may

The American Cancer Society's thinking is consistent with the FDA's approach to recognizing a continuum of risk, said Jeffrey Drope, ACS vice president of economic and health policy research.

"It is possible that e-cigarettes are saving lives (where there is complete switching), but also possible that they are costing some lives (dual use instead of quitting)," Drope said to The

"I think we're sort of vindicated that the growing science is pretty much consistent with our views," Abrams said. "Specifically, if you both look at the [NASEM] report and the science, e-cigarettes are saving lives, because the report concluded that they are substantially less harmful than cigarettes, and there is evidence that smokers who have completely switched to e-cigarettes are likely to have saved their lives.

"In other words, because they are much reduced-harm products and they are being used by smokers to switch or quit smoking, they save lives."

Abrams said NTRI's position doesn't differ from other public health organizations.

"We all say that the ideal is never to start using any form of nicotine, and if you do use, the ideal is to quit using it completely," Abrams said. "There's consensus that the only way to avoid all harm is to not expose yourself to any form of smoking and we agree on that.

"The perfection of ideally demanding that every smoker quits everything while eliminating harm—perfection is the enemy of pragmatic. The pragmatic is, but if you do use nicotine and can't stop, we hope you'll use a much less harmful product.

"Yes, ideally you'd maximize the harm reduction benefits by switching completely. However, what we don't know enough about is how do smokers use it and how much it takes for them to switch.

"The main thing you want to get across with the NASEM report and others is that smokers should absolutely try to find an e-cigarette that works for them if they can't quit completely."

NTRI does not receive any form of funding, Abrams said.

"We all are just feeling like we have to speak out, we have to educate the public about the options that they have, especially smokers who haven't been able to quit so far," Abrams said. "And so, we all do this completely out of our commitment to saving lives and public health.

"We haven't got any support from anybody, other than obviously like our universities—we're mostly academics or public health advocates with decades of senior leadership experience in tobacco and nicotine use behavior and therefore have the freedom to speak out."

Seffrin was not available for comment.

The text of NTRI's press release follows:

National Tobacco Reform Initiative

E-Cigarettes Are Saving Lives

ATLANTA, GEORGIA – January 30, 2018

The much anticipated NASEM report on e-cigarettes supports the FDA's bold new two-part nicotine strategy for product regulation: (1) reduce the addictiveness and appeal of deadly combustible cigarettes; and, (2) make safer alternative nicotine products available to addicted smokers.

There is an urgency to help smokers since 1 in 2 of them will die from a smoking-caused disease. This outcome can be prevented. Cigarettes and other combustible tobacco products are substantially more harmful than noncombustible tobacco and nicotine products, such as e-cigarettes.

The fundamental truth, that smoking—not nicotine—is responsible for the vast majority of the harm, and that smokers should have a variety of potentially less harmful nicotine-containing products if they want or need to continue using nicotine, is the keystone of FDA's approach.

A careful reading of the Report leads to the following evidence-based conclusions:

- E-cigarettes are significantly less dangerous than lethal tobacco smoke;
- To date, there simply is no evidence of long-term-use damage to the heart or lungs;
- E-cigarettes use can help smokers reduce their risk of certain lethal diseases;
- E-cigarettes use can and has helped many smokers quit tobacco smoking completely;
- E-cigarettes can help reduce the risk of lethal disease in smokers who either can't or won't quit smoking tobacco completely.

But, the Report also has lessons for public health advocates and officials outside of the FDA. We urge these professionals, within and outside government, to embrace the concept of relative risk. The science base clearly demonstrates that e-cigarettes represent less of a risk for smokers than continuing to smoke.

NTRI team member, John Seffrin, Ph.D., says: "After fighting the tobacco epidemic for over 5 decades, we now have proven harm reduction

methods to help us avoid a carnage in otherwise preventable deaths."

Now is the time to act:

- Approach regulation of tobacco and nicotine products according to their relative risk;
- Educate smokers that nicotine delivered without smoke is a less harmful choice and that there are massive differences in risk across the products;
- Pursue regulations that work to enable smokers to switch completely to the much less hazardous noncombustible products such as snus, and e-cigarettes.

The NAS Report and these evidence-based conclusions can help a consumer in making an informed choice about their use of nicotine products. This Report, along with FDA's comprehensive nicotine strategy, demonstrate that we know enough to tell smokers that the most important thing they can do to improve their health is to stop inhaling smoke from burning tobacco products (like cigarettes, cigars, roll-your-own) into their lungs, and if they continue to want to use nicotine, it is much better for their health to use it in a form that is not lit on fire and smoked.

David Abrams, Professor of Global Public Health at New York University, said: "Smokers have been horribly misled to believe e-cigarettes are as or are more harmful than smoking. The truth can reassure those who want to switch."

The National Tobacco Reform Initiative (NTRI) is serving as a catalyst to enhance smoking control nationwide, and to expand the dialogue on harm reduction. The NTRI Web Site provides further details on this important subject and on the Mission Statement, Priority Actions and current activities. The NTRI team is made up of 10 senior and independent national smoking control leaders who, collectively, have provided decades of service fighting the tobacco epidemic.

Further details on the NTRI, its Team of catalysts, advocates and conveners as well as the related Advisory Group of distinguished national public health leaders can be found on the NTRI Web Site.

SHOULD YOU HAVE QUESTIONS, PLEASE CONTACT DAVID ABRAMS; JOHN SEFFRIN, PH.D., OR ALLAN ERICKSON.

David Eaton
Chair of the National Academy of Sciences, Engineering and Medicine Committee on the Review of the Health Effects of Electronic Nicotine Delivery Systems, dean and vice provost of the Graduate School, and professor of environmental and occupational health sciences, School of Public Health at the University of Washington, Seattle

> While one might conclude from our report that a smoker who switches to e-cigarettes has reduced his/her risk, there is some uncertainty, and the evidence suggests that they must switch COMPLETELY.

The report does not say "e-cigarettes are saving lives", what it says is that there is:

1. Limited evidence that e-cigarettes may be effective aids to promote smoking cessation overall,
2. Moderate evidence from randomized controlled trials that e-cigarettes with nicotine are more effective than e-cigarettes without nicotine for smoking cessation;
3. Insufficient evidence from randomized controlled trials about the effectiveness of e-cigarettes as cessation aids compared with no treatment or to FDA–approved smoking cessation treatments;
4. Moderate evidence from observational studies that more frequent use of e-cigarettes is associated with increased likelihood of cessation.

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How FDA draws conclusions about the evidence that e-cigarettes 'saves lives' is of course up to them. What we've done is provided them with what we think is the strength of current scientific evidence regarding various aspects on the efficacy of e-cigarettes in reducing harm from tobacco products.

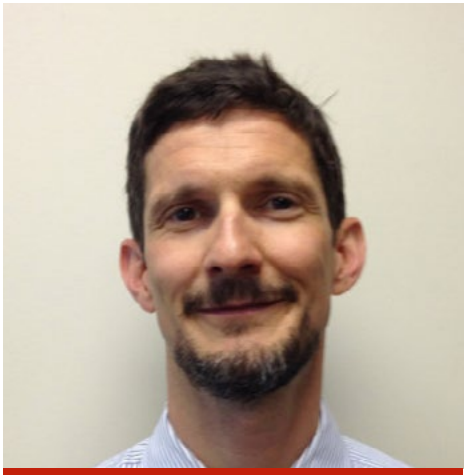
We did do some modeling that compares theoretical 'net public health impact' of e-cigarette use, based on various assumptions on:

1. relative 'harm' of e-cigarettes, compared to combustible tobacco products,
2. rates of 'smoking initiation' among youth/young adults from e-cigarettes, and
3. rates of smoking cessation (complete) among current adult smokers.

Nearly all of the modeling results, using assumptions for each of the three variables that could be considered reasonable and supported by current evidence, find a net public health benefit over the next 30 years (modeled to 2050), the magnitude of which decreases significantly by the year 2070. There are, however, some of the more extreme assumptions that resulted in theoretical net decreases in public health benefits, especially if they were assumed to have little or no effect on smoking cessation.

It is understandable how someone might interpret the modeling results as saying that 'e-cigarettes saves lives', but this is not what our report stated. The modeling of course is exactly that, and is totally dependent on the validity of the assumptions that go into the model, which are uncertain with our current state of knowledge.

While one might conclude from our report that a smoker who switches to e-cigarettes has reduced his/her risk, there is some uncertainty, and the evidence suggests that they must switch COMPLETELY (e.g., reduced risk from 'dual use' is uncertain).



Jeffrey Drope
Vice president of economic and health policy research at the American Cancer Society

> We must monitor this dynamic carefully to understand better the behaviors of young people, particularly their shifts among tobacco products. We do not want a new generation of young people addicted to nicotine products.

ACS will be releasing a statement soon about nicotine products more broadly that includes e-cigarettes. We strongly believe that these different tobacco products are interconnected and we must approach them in a comprehensive and sophisticated way that incorporates the principal complexities.

The levels of harm of these different products must certainly be one of those considerations, but it is only one of a number. In many ways, our approach and thinking are consistent with the FDA's approach to recognizing a continuum of risk.

As you know, a group of experts at ACS published a comprehensive review on electronic nicotine delivery systems (ENDS) last year and we had mostly similar findings to the NASEM report. For example, we found that the preponderance of evidence suggests strongly that the exclusive use of e-cigarettes is very likely to be less harmful than using combustible tobacco products (which includes dual use of e-cigarettes and conventional cigarettes).

Clearly, much of the harm from tobacco comes from inhaling the combusted product's smoke, which has particularly high levels of carcinogens and toxicants. It is important to note that the long-term effects of using non-combustible products such as e-cigarettes are simply not yet known.

We also found that there is reasonable evidence that e-cigarettes are helping some individuals to quit. Incidentally, we should note that it was beyond the purview of the NASEM report to examine cessation beyond e-cigarettes in much depth, so the report therefore lacks the broader context. This context is important because we find in our report that the government's and the public health/clinical communities' promotion and facilitation of FDA-approved cessation tools could be markedly improved.

This complicates a simple e-cigarette-focused scenario because obviously we have multiple tools at our disposal to fight tobacco use and drive down the harm it causes. Just because we have not effectively used some of the evidence-based tools already available to us (see CDC's Best Practices) does not mean we should abandon them or not make them one of our priorities.

It is possible that e-cigarettes are saving lives (where there is complete switching), but also possible that they are costing some lives (dual use instead of quitting). They have considerable potential to help smokers who cannot or will not otherwise quit using nicotine, thereby potentially producing a net public health benefit. But to accomplish that end, much work lies ahead—significant, effective public education and guidance to clinicians—and this must be managed in a responsible manner to avoid unintended consequences.

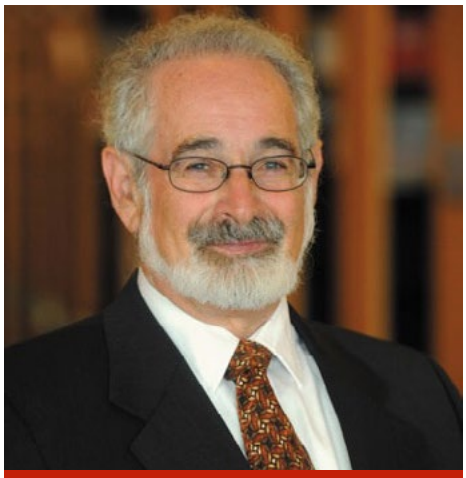
We share the concern about, but would like to see more research on, the NASEM report's findings of a strong association between youth who start using e-cigarettes and a greater likelihood of subsequently smoking conventional cigarettes. It is a far more complex relationship than the headlines suggest and difficult to tease out methodologically for reasons that we explore in our review.

That said, we must monitor this dynamic carefully to understand better the behaviors of young people, particularly their shifts among tobacco products. We do not want a new generation of young people addicted to nicotine products.

Broadly, we are carefully considering the net public health impact of e-cigarettes, which clearly depends on several factors, including youth e-cigarette initiation and adult smoking cessation, and the harm of e-cigarettes.

There is a key statement in the NASEM report worth citing here: "If e-cigarette use by adult smokers leads to long-term abstinence from combustible tobacco cigarettes, the benefit to public health could be considerable. Without that health benefit for adult smokers, e-cigarette use could cause considerable harm to public health in the short- and long-term due both to the inherent harms of exposure to e-cigarette toxicants and to the harms related to subsequent combustible tobacco use by those who begin using e-cigarettes in their youth."

Incidentally, we released a short statement on the report.



Stanton Glantz
Professor of medicine, the Truth Initiative Distinguished Professor of Tobacco Control, and director of the Center for Tobacco Research Control & Education at the University of California San Francisco

> The NAS report does say that switching completely to e-cigs would be less risky, a point most people (including me) agree with, but the reality is that complete switching is rare. Most e-cig users are dual users.

[NTRI] ignores the strong evidence (including in the NAS e-cig report) that e-cigs are expanding the tobacco market by attracting kids who are at very low risk of initiating nicotine use with cigarettes to e-cigarettes, many of whom go on to smoke cigarettes. Even if these kids do not progress to smoking, e-cigarette use is dangerous.

The statement misrepresents the conclusions in the NAS report about e-cigs and their effect on smokers' quitting. The actual report is ambivalent on this

point, noting that the studies are mixed. I think that even this is overly optimistic; the updated meta-analysis in the chapter I wrote for Annual Reviews of Public Health shows that, while some studies show increased quitting associated with e-cigs, overall smokers who use e-cigs are less likely to quit.

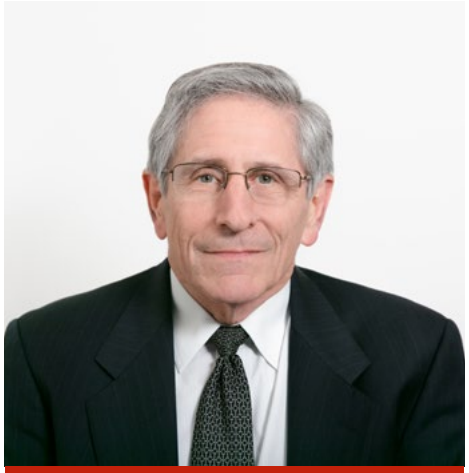
The NAS report does say that switching completely to e-cigs would be less risky, a point most people (including me) agree with, but the reality is that complete switching is rare. Most e-cig users are dual users.

Moreover, even this conclusion is coming into question. Recent research is showing that e-cigs turn on more inflammatory processes in the lung than conventional cigarettes.

Finally, the NTRI press release misrepresents the NAS conclusion that there is not YET information on long term health risks, that is quite different from a conclusions that there are no long term risks. It is simply too early to tell.

As time passes, the evidence for long term adverse effects is starting to grow. I will be presenting one such study at the Society for Research on Nicotine & Tobacco later this month.

The only way to convincingly reduce risk is to stop using tobacco products.



Matthew Myers
President, Campaign for Tobacco-Free Kids

> “FDA must ensure that any reduction in harm to individual tobacco users is not offset by increasing the number of people, including kids, who start using tobacco products or reducing the number of current tobacco users who quit.”

[NTRI's] characterization is an overstatement of the NASEM report findings. In fact, the chair of the committee that wrote the report stated that, based on the current evidence, “E-cigarettes cannot be simply categorized as either beneficial or harmful.”

The report underscores that many unanswered questions remain about the impact of e-cigarettes on public health, including their impact on smoking cessation, initiation of tobacco use by youth and health impact of long-term use:

- Cessation: The report found there is only “limited evidence that e-cigarettes may be effective aids to promote smoking cessation.” While noting there is “moderate evidence from observational studies that more frequent use of e-cigarettes is associated with increased likelihood of cessation,” it also concludes, “There is insufficient evidence from randomized controlled trials about the effectiveness of e-cigarettes as cessation aids compared with no treatment or to Food and Drug Administration-approved smoking cessation treatments.”

- Youth initiation: The report found there is “substantial evidence that e-cigarette use increases risk of ever using combustible tobacco cigarettes among youth and young adults.”

- Health impact: The report found that that the most critical scientific questions about the health effects of e-cigarette use remain unanswered. While smokers who switch completely to e-cigarettes reduce their exposure to toxic and carcinogenic substances, the report also finds, “There is conclusive evidence that in addition to nicotine, most e-cigarette products contain and emit numerous potentially toxic substances.” The report finds that while e-cigarettes are likely to be far less harmful

than conventional cigarettes, "the implications for long-term effects on morbidity and mortality are not yet clear" and there is insufficient evidence to draw meaningful conclusions about the risks e-cigarettes pose for diseases like cancer and heart disease.

The [NASEM] report does not say and cannot reasonably be interpreted to say that there is sufficient evidence to recommend that smokers switch to e-cigarettes as a primary mitigation strategy. Current law establishes an appropriate, science-based process for tobacco manufacturers to apply to the FDA to make claims that a product reduces harm or the risk of tobacco-related disease (called a "modified risk tobacco product").

Specifically, the law requires a company to demonstrate that the product "as it is actually used by consumers, will (A) significantly reduce harm and the risk of tobacco-related disease to individual tobacco users; and (B) benefit the health of the population as a whole," taking into account both users and non-users of tobacco products.

In other words, the FDA must ensure that any reduction in harm to individual tobacco users is not offset by increasing the number of people, including kids, who start using tobacco products or reducing the number of current tobacco users who quit. Manufacturers that want to make health claims about e-cigarettes should follow the law and provide the necessary scientific evidence to the FDA.

Effective FDA regulation is critical to minimizing the risks and realizing any potential benefits of e-cigarettes. FDA regulation is key to obtaining the information needed to provide the public and smokers with answers to the many questions about e-cigarettes, to prevent these products from undermining decades of progress in reducing youth smoking, and to assess which, if any, specific e-cigarettes at effective at helping smokers quit all tobacco products or switch completely away from cigarettes.

Aruni Bhatnagar
Professor of medicine, director of the Diabetes and Obesity Center at the University of Louisville, and fellow of the American Heart Association

> "E-cigarettes should not be viewed as the primary treatment for tobacco addiction when effective cessation treatments are available."

[NTRI's statement] is not an accurate interpretation. The NASEM report did not indicate or suggest that e-cigarettes are saving lives. It said that because there are fewer toxins in e-cigarettes, there may be less risk associated with their use compared to conventional cigarettes.

It's important to note that the committee stressed in the report and during their press briefing that there aren't any data that evaluate the long-term health effects of e-cigarettes or whether they save lives.

It is difficult to adopt a relative risk strategy for e-cigarettes when there isn't any evidence evaluating their long-term health effects. The body of research on e-cigarettes is far from complete, and much more study is needed.

Consequently, e-cigarettes should not be viewed as the primary treatment for tobacco addiction when effective cessation treatments are available. While these products may help adult smokers move away from more toxic conventional cigarettes, switching to e-cigarettes does not end your tobacco habit or your nicotine addiction.

E-cigarettes, like all tobacco products, present risk and the AHA is committed to ensuring that all American have access to cessation programs and products. Quitting all tobacco products should be the ultimate goal.

Q & A

Abrams spoke with Matthew Ong, a reporter with The Cancer Letter.

CONVERSATION WITH THE CANCER LETTER

NTRI's Abrams: Smokers should use e-cigarettes if they can't quit completely

> The perfection of ideally demanding that every smoker quits everything while eliminating harm—perfection is the enemy of pragmatic. The pragmatic is, but if you do use nicotine and can't stop, we hope you'll use a much less harmful product.

David Abrams
Professor, Department of Social and Behavioral Sciences at the New York University College of Global Public Health

Withholding e-cigarettes as an alternative from smokers who are unable to quit equals supporting the continued use of conventional cigarettes, said David Abrams, a member of the National Tobacco Reform Initiative.

"The main thing you want to get across with the NASEM report and others is that smokers should absolutely try to find an e-cigarette that works for them if they can't quit completely," said Abrams, professor, Department of Social and Behavioral Sciences at the New York University College of Global Public Health. "The public have been very much misled and wrongly believe that e-cigarettes would not help you quit."

Citing ideology and "old-school thinking," Abrams says regulators and other tobacco control advocates should stop being overly cautious and find a balance—by allowing some risks of e-cigarettes in order to save lives.

"I think the misinformation that is out there is a very big deal, and we hope public health leaders will now help correct misperceptions."

Abrams spoke with Matthew Ong, a reporter with The Cancer Letter.

Matthew Ong: When did you join the NTRI, and how did you become acquainted with the organization?

David Abrams: I joined pretty much at the beginning, maybe two years ago. I was sort of part of the group that—along with Allan Erickson and others—felt we needed a strong voice to look at how we might save more lives more quickly by embracing a harm reduction approach.

Could you describe the NTRI's position on e-cigarettes?

DA: I think we're encouraging a comprehensive look at all the science. The growing science is that e-cigarettes are dramatically less harmful than cigarettes. They do not burn tobacco. These newer products can deliver a satisfying alternative to combusted cigarettes and therefore they can be a vehicle for reducing the death and disease, which primarily comes from inhaling the smoke from combusting or burning the tobacco.

I've been very encouraged by the National Academy of Science report as well the latest Public Health England report that just came out days ago that are actually very consistent with the views we've held—embracing e-cigarettes as a dramatically less harmful alternative to cigarettes or any combusted smoke could save many more lives much more quickly than we've done up to now, with the technologies and alternative products that we've had today.

I think we're sort of vindicated that the growing science is pretty much consistent with our views.

The NTRI's press release on this issue led with "E-Cigarettes are Saving Lives." I checked in with David Eaton, the chair of the NASEM committee that authored the report. He said the report does not say or state that e-cigarettes are saving lives. Could you respond to that or clarify exactly what NTRI means by that statement?

DA: So, specifically, if you both look at the report and the science, e-cigarettes are saving lives, because the report concluded that they are substantially less harmful than cigarettes, and there is evidence that smokers who have completely switched to e-cigarettes are likely to have saved their lives. In other words, because they are much reduced-harm products and they are being used by smokers to switch or quit smoking, they save lives.

And by switching, do you mean a complete switch?

DA: Well, yes, ideally one would want to reduce harm as much as possible and that means not inhaling any of the toxins combusted in tobacco smoke, as one would get in cigarettes or little cigars or hookah, for example.

So, yes, ideally you'd maximize the harm reduction benefits by switching completely. However, what we don't know enough about is how do smokers use it and how much it takes for them to switch. We need more research about why some smokers can switch fairly quickly, exclusively; others take much longer, and so there's a period of co-use of both cigarettes and e-cigarettes where, obviously, you're not reducing your harm as much as you would if you switched exclusively.

However, there's also evidence from the FDA's PATH study, the [Population Assessment of Tobacco and Health Study] that found co-use does not increase the harms in the biomarkers of dual-use. Dual-use may well be a pathway to first reducing cigarettes and eventually switching. We just would recommend that one should cut down and eventually stop smoking even if it takes months or years to switch to maximize the harm reduction.

Is this the "relative risk" framework that the NTRI is advocating for?

DA: Yes. We embrace what FDA Commissioner [Scott] Gottlieb and Mitch Zeller, head of [FDA's Center for Tobacco Products] have stated very recently that there is a continuum of harm. I think Gottlieb and Zeller's NEJM article pretty much reframed the management of nicotine in America and embraced that the harm comes not from the nicotine itself—they literally say that, but from the combusted smoke and carbon monoxide in burning tobacco—and so, embracing a two-pronged approach, which is, let's make combusted tobacco products less appealing and obviously highly restrict cigarettes and all combusted tobacco products proportional to the fact that they are massively more harmful than any other mode of nicotine delivery.

They clearly stated the new nicotine management strategy for America was, at the same time, to make smoked tobacco less appealing and to support alternative, less harmful products for those smokers who are unable to quit or wish to continue using nicotine and just can't quit.

So for those people, we would obviously have this risk proportional to the harm of each class of product with smoked tobacco being overwhelmingly so much more harmful. Regulation and nicotine use policy should all be proportional to the risk-ratio of the product class. And again, that means massively discouraging use of smoked tobacco and encouraging the innovation that would lead to satisfying alternatives for smokers who do not want to quit or cannot quit.

It seems the majority of public health organizations tend to focus of complete cessation instead of saying that e-cigarettes are a way of getting there. What sets NTRI apart?

DA: I don't think there's a difference. We all say that the ideal is never to start using any form of nicotine, and if you do use, the ideal is to quit using completely. There's consensus that the only way to avoid all harm is to not expose yourself to any form of smoking and we agree on that.

However, we are more pragmatic, I think, as has been demonstrated in science of behavior and it's often resisted before it's embraced, and that's the concept of harm reduction.

It was resisted when Surgeon General Everett Koop spoke out about the AIDS epidemic and people did not want him to say, "You know, IF you are engaging in risky behavior; here are ways to reduce your harm." To his credit, he became a leader that saved millions of people in America by embracing harm reduction.

The perfection of ideally demanding that every smoker quits everything while eliminating harm—perfection is the enemy of pragmatic. The pragmatic is, but if you do use nicotine and can't stop, we hope you'll use a much less harmful product. These products are now available—at least you should find one and switch, rather than you just smoke because you can't quit.

So I think, Americans, we just feel the harm reduction alternative of these new innovative products has not been embraced as another way to reduce the death and disease. We're also embracing the surgeon general's report that said everything we're doing is too slow. We've had a lot of success, but we still have 40 million smokers and everything we have done so far has not accelerated cessation. Here are some alternatives that might save many more lives more quickly. So it's a complement to the model that says, "Ideally, you should not use anything." It's to say, "If you are using, choose a less harmful product."

What does NTRI's funding look like?

DA: There is no funding. We all are just feeling like we have to speak out, we have to educate the public about the options that they have, especially smokers who haven't been able to quit so far. And so, we all do this completely out of our commitment to saving lives and public health. We haven't got any support from anybody, other than obviously like our universities—we're mostly academics or public health advocates with decades of senior leadership experience in tobacco and nicotine use behavior and therefore have the freedom to speak out.

I have to say, we just saw the [Health Information National Trends Survey] data from the National Cancer Institute which came out last week, and we are devastatingly disappointed that the public this year are even more convinced that e-cigarettes are equally harmful as cigarettes or more harmful. The misperception has actually gone the wrong way.

I think, in the HINTS data, almost half of all smokers believe that e-cigarettes are as harmful as cigarettes. I think that misperception is discouraging them from trying to quit, using e-cigarettes and discouraging them from exclusively switching, because they are so confused about where the e-cigarettes are—the correct answer is they are much less harmful, and e-cig-

arettes are not just a little less harmful, or equally harmful or more harmful.

And so, we're trying to massively correct public perception, because now, NASEM, Public Health England, and several other reports are all in agreement that they're substantially less harmful. The public is confused because we've seen so many exaggerated headlines of small studies that pick on one toxicant and exaggerates the harms and fail to include a statement of that vaping overall is still substantially less harmful than smoking. The public doesn't understand overall these products that do not burn tobacco are substantially less harmful.

So I think some of the problem is that the even more benefit and much more exclusive switching would happen if the public were told the whole truth that A) e-cigarettes are substantially less harmful, and B) that they can help you quit if you find one that works for you and persist in using it long enough to allow your brain to get used to it and then you can reduce and eventually eliminate your smoking of cigarettes.

That whole process, I think, is confusing, and the public have been very much misled and wrongly believe that e-cigarettes would not help you quit.

The main thing you want to get across with the NASEM report and others is that smokers should absolutely try to find an e-cigarette that works for them if they can't quit completely. But I think the misinformation that is out there is a very big deal, and we hope public health leaders will now help correct misperceptions.

Is NTRI in any way related to the Foundation for a Smoke-Free World?

DA: Not at all, absolutely not. None of us are on the foundation other than Derek Yach. He is a member of our group and as an individual has input in what we do. I think actually, Derek may be the only member that's currently associated with the foundation. There's no one else that I'm aware of in NTRI that has any affiliation with that foundation.

Did I miss anything?

DA: No, I just would hope that The Cancer Letter provides a more balanced view of what the science actually says. Frankly, I do think, in the past there has been what we call the "precautionary principle," which I think has been applied.

It's a little esoteric, but I think it's really important, and actually, I quote Sir Francis Bacon on how ideology and prior old-school thinking can color and distort the current reality, because some people are ultimately embracing the precautionary principle, and what that is, is when we have doubts, therefore, we should be very conservative and we cannot support e-cigarettes.

Obviously, that's changed, because the science is there now, but I think there's still this lingering worldview that the precautionary principle should be embraced, because we're a little unsure of the long-term effect and obviously, we're all concerned that we wouldn't want kids to be attracted to a novel new product and then progress to cigarette smoking, and we all share that concern.

But I think it's important to think about the following and it's brought out beautifully in the Public Health England report. It's actually very similar to the concerns about the HIV/AIDS movement that led ultimately to FDA modifying the way it reviewed and expedited new drugs when the harm is so high that there's an urgent request or desire to have a drug approved, even when some of its effects are unknown.

It came out of, I think, the very correct view that when death and disease are very, very high, there's an urgency to think about the precautionary principle a little differently. In other words, when a disease is killing people quickly and you have inadequate alternatives, you're better off allowing some risks of a new product in order to save lives.

Since the smoke from burning tobacco leaves kills prematurely more than half of lifetime smokers, withholding a promising intervention that might saves their lives when we don't have perfect science in terms of the harms, and even being willing to take some risks because of the urgency, you can overstate the precautionary principle and use it, in fact, in a way that withholds a really good alternative for smokers who are unable to quit and, in so doing, you are in fact unwittingly supporting the continued use of deadly cigarettes.

So, the abundance of caution inadvertently slows their ability to save their lives. The precautionary principle is inverted when information about new products that are less harmful is withheld from the public out of an abundance of caution.

That's the opposite of the precautionary principle, and there's a whole section on that in the Public Health England report, that balance must be found between legitimate precaution and being overly cautious that then withholds a very helpful lifesaving intervention from the public or discourages it's use.

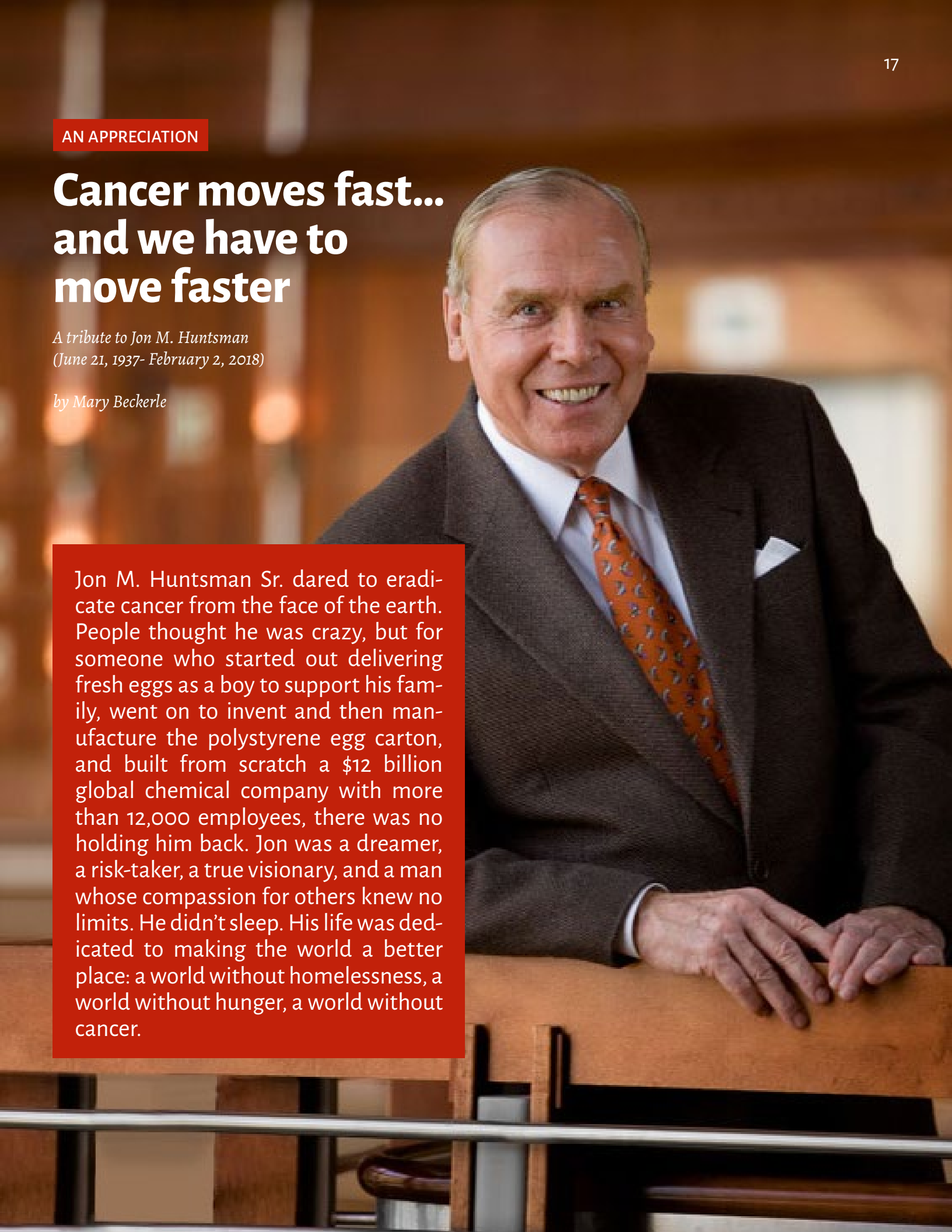
One has to be very careful about how one plays out the precautionary principle when so many lives are being lost so quickly, we still have 40 million smokers—that kind of thing.

AN APPRECIATION

Cancer moves fast... and we have to move faster

A tribute to Jon M. Huntsman
(June 21, 1937- February 2, 2018)

by Mary Beckerle



Jon M. Huntsman Sr. dared to eradicate cancer from the face of the earth. People thought he was crazy, but for someone who started out delivering fresh eggs as a boy to support his family, went on to invent and then manufacture the polystyrene egg carton, and built from scratch a $12 billion global chemical company with more than 12,000 employees, there was no holding him back. Jon was a dreamer, a risk-taker, a true visionary, and a man whose compassion for others knew no limits. He didn't sleep. His life was dedicated to making the world a better place: a world without homelessness, a world without hunger, a world without cancer.

From left to right: Mark, Jon, and Karen Huntsman at the dedication of the Primary Children's and Families' Cancer Research Center at Huntsman Cancer Institute. The building was dedicated on Jon Huntsman's 80th birthday.

He died peacefully at home on Friday, February 2, 2018, surrounded by his family.

Just a few months ago, on June 21, 2017, we celebrated Jon's 80th birthday. And what a magnificent 80 years it has been. From class president, to the U.S. Navy, to the White House as special assistant to a President, to leadership in The Church of Jesus Christ of Latter-day Saints (the Mormon church), to Chairman of the Board of Huntsman Corporation, to international recognition and appreciation for his philanthropy.

Jon was born poor in Idaho, and spent his early childhood in a two-room home that didn't have indoor plumbing. His family moved around a lot in the early days and Jon worked odd jobs—mowing lawns, delivering newspapers. He may not have realized it at the time, but he was well on his way to becoming an entrepreneur: nine-year-old Jon would buy newspapers for three cents each, then promptly turn around and sell them for five.

After graduating from Palo Alto High School, Jon received a scholarship to attend the Wharton School at the University of Pennsylvania. From what I've heard from one of his classmates, he had a lot of fun at Penn, and also picked up a strong business education along the way. After college, he married his high school sweetheart, Karen Haight, and started a family that ultimately grew to 9 children, and a current count of 56 grandchildren and 26 great-grandchildren. The table at the Huntsman family home in Salt Lake City is welcoming and large.

Around that table, Jon taught his children about leadership and about giving back. Earlier this year, Jon told me that he emphasized two key principles to his children as they sat in their "boardroom": "Check your ego at the door" and "Be your sibling's best cheerleader."

He modeled generosity and service: whether it was rebuilding Armenia after a devastating earthquake, adding a new facility to the Wharton School or the Jon M. Huntsman School of Business at Utah State University, building a shelter for abused women and children

The Jon M. and Karen Huntsman family, taken in 2016

at the Salt Lake City YWCA, supporting college scholarships or the Special Olympics. So many areas in addition to his primary focus and passion: cancer.

Cancer didn't wait long to touch Jon Huntsman. Breast cancer took his mother, Kathleen Robison Huntsman, who died in his arms in 1969. Pancreatic cancer took his brother, Blaine. Jon's father died of prostate cancer in 1991 and, later that same year, Jon was diagnosed with prostate cancer. Jon's sons often quip that they hope they inherited their mother's prostate. They can joke about it now, but back then it was no laughing matter. Jon recalled being "terrified" at the time.

Karen Huntsman was concerned when her husband showed up at home in the middle of the day—something very unusual for him on a workday. He was there to tell her he had cancer. They didn't know where to turn.

After successfully navigating the confusion and fear of that first cancer journey, Jon and Karen decided they never wanted anyone else to have to experience what they had. Jon was eyeing the open hillside, with flowing amber grasses at the east side of the University of Utah campus. He envisioned a "cancer campus" with cutting edge research, compassionate and state-of-the-art clinical care, and a learning center to educate patients and the public about cancer risk, prevention, and care.

In 1993, Jon established the Huntsman Cancer Institute at the University of Utah. Two years later, he announced a $100 million donation to support cancer research. At the time, this was the largest gift ever given by a single individual to support medical research and the second largest cash gift in the history of American higher education. Many hundreds of millions more would follow.

Jon took his case for cancer to anyone who would listen. He walked the halls of Congress advocating for cancer research funding, saying that he was non-partisan—he was with "The Cancer Party." He sweetly and effectively twisted arms of friends, relatives, acquaintances, and people he barely

knew to garner support for cancer research. Jon Huntsman was on a mission. More than a million individual donors joined the cause.

The first Huntsman Cancer Institute facility opened in 1999. As soon as plans were completed for one phase, Jon was already envisioning the next—and everyone around him was trying to keep up.

In 2004, a 50-bed cancer specialty hospital; in 2011, a major expansion doubled the size of the cancer hospital; in 2017 a doubling of the Institute's research space. A million square feet, dedicated to healing and hope; a National Cancer Institute-designated Comprehensive Cancer Center serving the five-state Mountain West, a vast geographic region that spans 17% of the landmass of the continental USA.

People like to say that the cancer hospital at HCI was the first cancer hospital designed by a patient. We may never know if that's true, but it is indisputable that Jon's experiences as a cancer patient in 1991 shaped the architecture and aesthetic at HCI.

He recalled the dark interior hallways that led to his treatment rooms back in 1991; at HCI he created an inspiring, light-filled cancer hospital with natural wood and stone and easy visual wayfinding. He recalled the terrible hospital food that came when he wasn't hungry; at HCI he built a wood fired pizza oven and room service for patients and their families.

He recalled the sterile and lonely environment; at HCI he furnished hospital rooms with extra beds for family members, donated a museum-quality collection of American Indian artwork that graces treatment and waiting areas, built a private outdoor patio off of an inpatient floor so nature and a mountain view are accessible to all.

Ever the practical businessman, he created a business center so family members could keep their work going while living at the hospital.

Jon dedicated his life to the goal of eliminating the suffering caused by cancer. And he didn't leave this life until he was confident that the future of his beloved cancer center was secure.

In 2017, he and his son, Peter, negotiated a new agreement with the University of Utah that ensures that HCI will always oversee an integrated three-fold mission of research, clinical care, and education/outreach. He secured the financial future of HCI. And, importantly, before he left us, he passed the torch to the next generation of his family, ensuring an enduring partnership and commitment until such time as Jon's dream of eradicating cancer is fulfilled.

Jon always said that we would then turn Huntsman Cancer Institute into a Ritz-Carlton resort.

Everyone has a story about Jon Huntsman. I heard several new ones at an impromptu community gathering at HCI, three days after his passing. An employee told us that when his brother-in-law passed away, Jon, Karen, and their son, Markie, travelled to their small town in Idaho to express their sympathies and let the family know that the educations for all of the children would be fully taken care of (Jon of course kept his word).

One of our oncologists made us all smile when describing how Jon, upon learning that the doctor was a vegetarian, spent time reassuring him that the cancer institute's restaurant would soon have a salad bar.

As CEO of HCI, I quickly learned to plan an extra thirty minutes when Jon and I walked from my office to the cancer hospital—normally a 2-minute stroll—because Jon would stop, or be stopped, every few steps to greet someone by name, ask about their family, hug a patient, cheer them on.

When someone is such a public figure, and such a generous philanthropist, they rightly are known for their important contributions to society. But it is the everyday humanity, the myriad acts of kindness, the courage it takes to do something that is truly meaningful that made this man. As Jon says: "Cancer moves fast… and we have to move faster." And we will.

The author is the CEO and director of Huntsman Cancer Institute at the University of Utah

Congress passes two-year budget deal, paving the way toward giving NIH a $2 billion raise

By Paul Goldberg

So, the federal government shut down while America slept, but it reopened after a five-and-a-half hour pause, by early morning Feb. 9. We've seen this dance before.

However, in a move that is anything but yawn-inducing, Congress passed a budget deal that paves the way toward giving NIH a $2 billion raise and lifts the spending caps on defense and non-defense spending through March 2019.

The deal, which President Trump had signed into law, will fund federal agencies through March 23, giving Congressional appropriators the breathing room to put together a $1.3 trillion omnibus spending bill that would fund the government through the end of the fiscal year on Sept. 30.

The brief shutdown was triggered by Sen. Rand Paul (R-KY), who sought to delay the vote on the continuing resolution. Paul objected to deficit spending allowed in the measure. The bill ultimately passed 71 to 28 in the Senate and 240 to 186 in the Senate.

This stopgap spending bill is significant because Republican-controlled Congress, in—yes—a bipartisan manner, has overruled an effort by the Trump White House to slash the NIH budget by 21 percent (The Cancer Letter, March 17, 2017; April 7, 2017; May 26, 2017).

Under President proposal, indirect costs would have been capped at 10 percent, a level that would have crippled research at academic institutions (The Cancer Letter, March 2, 2017).

The proposal energized the NIH supporters on both sides of the aisle, and instead of the cut, Congressional bills ended up giving NIH a $2 billion increase (The Cancer Letter, June 23, 2017; March 17, 2017; May 5, 2017). The indirect costs provision didn't make it into the bill.

The White House is expected to release its budget proposal for FY 2019 on Feb. 12. After Congress lifted the spending caps, the Office of Management and Budget said that the proposal would still come out as scheduled. However, the document will be published with an addendum, which will reflect the new spending caps.

In an email quoted by CQ, a senior administration official wrote that "simultaneous with our release of the budget, we will release an addendum laying out the Administration's roadmap for how to account for the increased spending caps in a responsible manner." The addendum will "include additional FY19 funding for a limited set of Administration priorities as well as proposals to fix certain budget gimmicks used to circumvent the spending caps. Separate from our FY19 budget request and addendum, we will also be providing technical assistance to Congress on how we recommend Congress allocate funding under the increased FY18 caps."

It's not publicly known how much the White House proposal initially intended to give NIH and whether this proposed level has changed as a result of the budget deal.

"The House and Senate passage of the 'Bipartisan Budget Act of 2018,' which adds $296 billion in discretionary funding for fiscal year 2018—which began Oct. 1—and FY 2019, paves the way for the NIH to receive a $2 billion funding increase in FY 2018, which is what was approved last year by the Senate Appropriations Committee. The two-year agreement to raise the budget caps also provides the foundation for the NIH to realize another $2 billion + budget increase in FY 2019," said Jon Retzlaff, chief policy officer for the American Association for Cancer Research. "This wonderful bipartisan agreement will allow our four passionate and determined champions for medical research [Senate Appropriations Subcommittee Chairman Roy Blunt (R-MO), House Appropriations Subcommittee Chairman Tom Cole (R-OK), and the two respective Ranking Members, Senator Patty Murray (D-WA) and Congresswoman Rosa DeLauro (D-CT)], to continue to lead the charge and ensure that the NIH remains a national priority. Their actions are allowing our nation's researchers and physician-scientists to significantly accelerate the pace of progress against cancer, as well as any number of the hundreds of other diseases that afflict millions of Americans."

"This bipartisan budget deal provides a crucial opportunity to re-energize our national commitment to research, innovation and other priorities essential to the health and well-being of Americans," Mary Woolley, president and CEO of Research!America, said in a statement. "We are grateful that the agreement provides for at least $2 billion in additional funding for the National Institutes of Health over a two-year period. In order to combat major health threats ranging from Alzheimer's disease, cancer to the deadly flu epidemic, the NIH and other health agencies require robust funding to confront these challenges head-on."

Chris Hansen, president of the American Cancer Society Cancer Action Network said that "consistent and sustainable funding increases for the NIH are essential to ensuring researchers can keep innovating and developing new potentially lifesaving diagnostic tests, treatments and therapies for diseases like cancer.

"In addition, Congress should maintain funding for cancer prevention and screening programs at the Centers for Disease Control and for important tobacco cessation programs through the Office of Smoking and Health," Hansen said.

"The decision to fund Federally Qualified Health Care Centers (FQHCs) for two years and further extend funding for the Children's Health Insurance Program (CHIP) for an additional four years will provide peace of mind to millions of low-income adults and children, including many cancer patients, who rely on these programs for critical health care services.

"While this deal addresses a number of critical federal programs that are instrumental in making progress against cancer, ACS CAN is disappointed that the legislation cuts the Prevention and Public Health Fund by $1.35 billion as an offset for spending. Funding for effective prevention programs is critical to reducing death and suffering from cancer, a disease that continues to kill 1,650 people a day in this country."

The measure extends funding for the Children's Health Insurance Program for four more years, ensuring the program will be funded through 2028, but doesn't address the situation of an estimated 700,000 "Dreamers," children of undocumented immigrants who were brought to this country illegally.

CRUK names ten finalists for £20m Grand Challenge

Cancer Research UK has shortlisted ten multidisciplinary, international teams for what amounts to the second leg of competition for Grand Challenge awards.

Each of the teams will now receive £30,000 in seed funding to prepare up their applications for interviews later this year.

They are competing for the £20m Grand Challenge funding award (The Cancer Letter, July 21).

The ten team were chosen from a pool of 134 applications from 41 countries.

The challenge, now in its second phase, plans to give out several £20 million awards over five years to researchers who would be willing to address one of eight challenge areas.

The strategy—borrowed from mathematics—is to identify the most significant barriers to making progress and challenge scientists all over the world to join forces to answer them. The Grand Challenge provides the largest single response-mode grants available in cancer research, CRUK said.

The approach of focusing the attention of an entire discipline on a specific set of questions originated with David Hilbert, a German mathematician. In 1900, Hilbert identified 23 problems and presented 10 of them at the Paris conference of the International Congress of Mathematicians. His list of challenges had in effect set the course for research in mathematics through much of the 20th century.

Winners will be determined by a panel that includes:

Richard Klausner, a biotechnology entrepreneur, former NCI director, and chair of the Grand Challenge advisory panel;

Adrian Bird, the Buchanan Professor of Genetics at the University of Edinburgh;

Suzanne Cory, of the Walter and Eliza Hall Institute of Medical Research;

Ed Harlow, professor of Biological Chemistry and Molecular Pharmacology at Harvard Medical School;

David Lane, chief scientist of the Agency for Science, Technology and Research (A*STAR) in Singapore, scientific director of Ludwig Cancer Research, and chairman of Chugai Pharmabody;

Christopher Wild, director of the International Agency for Research on Cancer;

René Bernards, professor of molecular carcinogenesis at Utrecht University and head of the section of molecular carcinogenesis at the Netherlands Cancer Institute-Antoni van Leeuwenhoekziekenuis;

Brian Druker, director of OHSU's Knight Cancer Institute, Jeld-Wen Chair of Leukemia Research;

Nic Jones, professor and director, CRUK Manchester Centre; and

Elizabeth Jaffee, deputy director of the Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins, the Dana and Albert "Cubby" Broccoli professor of oncology, and professor of pathology at the Johns Hopkins University School of Medicine.

The Round 2 shortlisted teams are:

Uncovering how obesity causes cancer

Lead: Dr Meritxell Huch
Grand Challenge: Cancer Causes
Countries: Austria, The Netherlands, UK and USA

Dr Huch's team want to investigate what's happening inside our cells when they are exposed to too much fat, and how that can lead to cancer.

This team is made up of biologists, clinicians, geneticists, pathologists and physicists.

Unravelling how chronic inflammation causes cancer

Lead: Professor Rong Li
Grand Challenge: Cancer Causes
Countries: UK and USA

Professor Li's team want to scrutinise people's DNA in supreme detail to find out how inflammation can damage or alter a cell's chromosomes, and then define how this can lead to cancer.

This team is made up of of biologists, bioengineers, geneticists and epidemiologists.

A new way to tackle inflammation-associated cancer

Lead: Professor Thea Tlsty
Grand Challenge: Cancer Causes
Countries: Canada, Israel, UK and USA

Professor Tlsty's team want to find novel ways of treating cancer that has been caused by inflammation, and develop new options to prevent cancer developing in high-risk patients with chronic inflammatory diseases.

This team is made up of pathologists, system biologists, bioengineers, gastroenterologists, microbiologists, immunologists and biologists.

Looking out for cancer

Lead: Dr Trevor Esward and Professor Sara Faithfull
Grand Challenge: Artificial Intelligence
Countries: The Netherlands and UK

Dr Trevor Esward and Professor Sara Faithfull's team want to analyse people's consumer and behavioural habits for clues that might indicate if a person has cancer and to address the ethical and privacy issues of accessing personal data.

This team is made up of physicists, clinical innovators, data scientists, health policy experts, clinical oncologist, academic lawyers and health informaticians.

Mining medical records for early signs of cancer

Lead: Professor Henk van Weert
Grand Challenge: Artificial Intelligence
Countries: Denmark, The Netherlands and UK

Professor van Weert's team want to use machine-learning technology to mine electronic health records and public databases for clues that could help GPs identify patients that are showing early signs of cancer.

This team is made up of GPs, informaticians, epidemiologists, psychologists and neuroscientists.

Eliminating sleeping cancer cells

Lead: Professor Peter Croucher
Grand Challenge: Dormancy
Countries: Australia, Israel, UK and USA

Professor Croucher's team want to create a map of the biological environment around dormant cancer cells and the processes that control them, so that treatments can be developed to stop cancer returning.

This team is made up of biologists, immunologists, geneticists, haematologists and epigeneticists.

Eradicating tumours with personalised cancer vaccines

Lead: Professor Lindy Durrant
Grand Challenge: Tumour Vaccinology
Countries: Germany, The Netherlands, UK and USA

Professor Durrant's team want to build vaccine templates for how to treat different cancers, with the hope that eventually cancer patients will be offered a vaccine that is specifically designed for their unique tumour.

This team is made up of immunologists, surgeons, neuroimmunologists, biologists and clinicians.

Dissecting the tissue specificity of cancer drivers

Lead: Professor Stephen Elledge
Grand Challenge: Tissue Specificity
Countries: The Netherlands and USA

Professor Elledge's team want to generate a comprehensive map of cancer drivers and their specificity to different tissues. This has the potential to improve our basic understanding of cancer, and provide information that will impact therapeutic choices for patients.

This team is made up of geneticists, clinicians and bioinformaticians.

Working smarter, not harder: improving treatment combinations

Lead: Professor Jean-Pascal Machiels and Dr Anthony Kong
Grand Challenge: Treatment Regimens
Countries: Belgium, Denmark, Germany, Ireland, Italy and UK

Professor Jean-Pascal Machiels and Dr Anthony Kong's team want to use artificial intelligence and computer modelling to determine the optimum treatment combination for each individual patient, transforming outcomes on a global scale.

This team is made up of clinicians, bioinformaticians, biologists, immunologists and mathematicians.

Bugs, guts & cells: beating gastrointestinal cancer

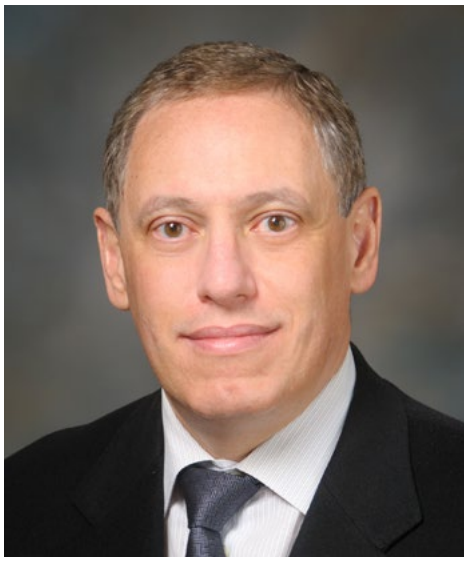
Lead: Professor Matthew Meyerson
Grand Challenge: Microbiota
Countries: Canada, The Netherlands, Spain, UK and USA

Professor Meyerson's team want to discover exactly how certain microbes inside the body lead to cancer development and influence a patient's response to treatment.

This team is made up of genomicists, microbiologists, geneticists, immunologists, biologists, epidemiologists and pathologists.

IN BRIEF

Arap, Pasqualini named to leadership posts at Rutgers Cancer Institute of New Jersey at University Hospital in Newark



Wadih Arap was named director of Rutgers Cancer Institute of New Jersey at University Hospital.

Previously, Arap served as chief of the Hematology/Oncology Division and deputy director of the University of New Mexico Comprehensive Cancer Center. Upon arrival to the Newark facility, Arap assumed the director role from Susan Goodin, professor of medicine at Rutgers Robert Wood Johnson Medical School, who served in an interim capacity.

Arap also will serve as chief in the Division of Hematology/Oncology in the Department of Medicine at Rutgers New Jersey Medical School.

Since 2016, the multidisciplinary cancer service line at University Hospital in Newark has included care provided by Rutgers Cancer Institute medical and surgical oncologists augmenting radiation oncology services which have been provided there since 2009.

"Dr. Arap's research and clinical expertise complements the mission of Rutgers Cancer Institute—the state's only NCI-designated Comprehensive Cancer Center," said Rutgers Cancer Institute Director Steven Libutti, who is also senior vice president of oncology services at RWJBarnabas Health and vice chancellor for cancer programs for Rutgers Biomedical and Health Sciences.

Adding to the leadership on the Newark campus, Renata Pasqualini was named chief of the Division of Cancer Biology in the Department of Radiation Oncology at Rutgers New Jersey Medical School. Prior to her new role, Pasqualini served as associate director for translational research and chief of the Division of Molecular Medicine at the University of New Mexico Comprehensive Cancer Center.

Pasqualini and Arap, a husband-and-wife team, have led a joint laboratory program for 20 years. Each has previously held leadership positions during their 14-year tenure at the University of Texas MD Anderson Cancer Center.

Together, they developed a system to identify different molecular signatures based on where they are located in the body. They showed that these so-called "vascular ZIP codes" may be used to selectively deliver therapeutic and diagnostic agents in diseases such as cancer, obesity, and blinding eye disorders.

Dhodapkar named director of new Center for Cancer Immunology at Emory Winship

Madhav Dhodapkar, an expert in cancer immunology and translational immunotherapy, will join Winship Cancer Institute of Emory University on March 1 as the director of the new Winship Center for Cancer Immunology.

He will be appointed as the Anise McDaniel Brock Chair and Georgia Research Alliance Eminent Scholar in Cancer Innovation and professor in the Department of Hematology and Medical Oncology in the Emory School of Medicine.

For the past decade, Dhodapkar has served as chief of hematology, the Arthur H. and Isabel Bunker Professor of Medicine (Hematology), and professor of immunobiology at Yale University School of Medicine. An expert in the treatment of multiple myeloma, he also was co-director of the Cancer Immunology Program within the Yale Cancer Center.

Dhodapkar is credited with helping define the role of the immune system in controlling early cancer cells. His research focuses on how the immune system regulates the progression from precursor lesions to cancer as well as the mechanisms of treatment sensitivity and resistance to cancer immunotherapy.

Dhodapkar's wife, Kavita Dhodapkar, MBBS, a leading cancer immunology

researcher at Yale, will also join the Emory faculty as an associate professor in pediatrics and director of the Pediatric Immuno-Oncology Program at the Aflac Cancer and Blood Disorders Center at Children's Healthcare of Atlanta. She will also become an active Winship investigator in cancer immunology.

Oberstein named director of GI medical oncology at NYU Perlmutter Cancer Center

Paul Oberstein will join NYU Langone Health and its Perlmutter Cancer Center March 1 as director of gastrointestinal medical oncology and assistant director of its recently established Pancreatic Cancer Center.

Prior to his post at NYU Langone, Oberstein was a member of the Herbert Irving Comprehensive Cancer Center at Columbia University, an assistant professor at Columbia University College of Physicians & Surgeons and an attending physician at New York-Presbyterian/Columbia University Medical Center.

Oberstein's research focuses on the design and implementation of translational studies that apply novel laboratory concepts to patients.

His recent work includes biomarker research to understand the immune microenvironment of cancer cells, investigation of a new imaging method for detecting pancreatic tumors, and testing new combinations of chemotherapy and immunotherapy in advanced pancreas cancer patients. Oberstein also will see patients and expedite the progression of laboratory studies and research on all types of GI cancers to clinical practice.

Campbell joins Fox Chase Cancer Center Cancer Biology Program

Paul Campbell has joined Fox Chase Cancer Center as an assistant professor in the Cancer Biology Program.

Campbell comes to Fox Chase from the Drexel University College of Medicine, where he led his own lab focusing on cancer cell signaling. The Campbell lab studied cell systems, with a particular interest in tumorigenesis driven by the activation of the protooncogene K-Ras.

At Fox Chase, Campbell's research will continue to focus on the signaling that drives cancer progression, invasion, and metastasis, with the overall objective of discovering and validating new targets for drug development and finding novel biomarkers for earlier detection and therapeutic monitoring.

IU gets $14 million gift to create program focused on symptom management

Indiana University School of Medicine received a $14 million gift from the Walther Cancer Foundation to create a supportive oncology program that goes beyond standard therapies such as surgery, chemotherapy, and radiation.

The program, named the Walther Supportive Oncology Program, will seek to care for a patient's overall physical, mental and spiritual well-being.

As part of For All: The Indiana University Bicentennial Campaign, the gift will receive matching funds from Indiana University.

The Walther Supportive Oncology Program will be developed in partnership with Indiana University Health. It is also intended to influence care for cancer patients and their families throughout Indiana and the country by providing expertise and best-practices for other health systems to model, with particular attention to the underserved in our communities.

The gift from Walther is establishing five endowed faculty positions that will enable IU School of Medicine to hire a nationally recognized leader in the field of supportive oncology to direct the program; a senior leader in psychiatry or psychology who focuses on individuals with cancer; and at least three other faculty experts in related disciplines. As part of the program, IU Health and IU School of Medicine will invest in additional staff to complement existing services.

The Walther Supportive Oncology Program will also place an emphasis on research in areas such as physician-patient communication, care coordination, symptom management and the long-term effects of cancer on survivors. This includes laboratory research to predict which patients will suffer side effects to specific therapies and how to mediate them, and to discover treatments that are less toxic.

The program will also include an educational component to train the next generation of clinical leaders in supportive oncology.

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THE CLINICAL CANCER LETTER

CLINICAL ROUNDUP

In phase III study Tecentriq and Avastin reduced risk of disease worsening/ death by 26 percent in advanced kidney cancer

Genentech announced results from the positive phase III IMmotion151 study of Tecentriq (atezolizumab) and Avastin (bevacizumab) as a first-line treatment for advanced or metastatic renal cell carcinoma.

The study met its co-primary endpoint of investigator-assessed progression-free survival in people whose disease expressed the PD-L1 (expression ≥ 1 percent) protein. Those who received Tecentriq plus Avastin had a 26-percent reduced risk of disease worsening or death compared to people treated with sunitinib (median PFS [mPFS]: 11.2 vs. 7.7 months; HR=0.74; 95 percent CI 0.57, 0.96; p=0.02).

Initial observations from the co-primary endpoint of overall survival in the overall study population (intention-to-treat) are still immature. Safety for the Tecentriq and Avastin combination appeared consistent with the known safety profile of the individual medicines and what was previously reported in the phase II IMmotion150 study.

No new safety signals were identified with the combination. The rate of treatment-related grade III-IV adverse events was lower with the Tecentriq and Avastin combination (40 percent) than with sunitinib alone (54 percent) in all treated patients.

Observations of a pre-specified subgroup analysis of the Tecentriq and Avastin combination indicated that, in people whose disease expressed PD-L1, a numerical difference in PFS favoring Tecentriq was seen across all patient risk factor groups (favorable, intermediate and poor) compared to sunitinib.

In addition, a pre-defined analysis of patient-reported outcomes revealed that the combination of Tecentriq and Avastin markedly delayed the time to a worsening of disease symptoms that interfere with day-to-day life compared to sunitinib, (median time to deterioration: 11.3 vs. 4.3 months; HR=0.56; 95 percent CI: 0.46, 0.68) in the ITT population. Due to the study design, pre-defined subgroup analyses and pre-defined PRO analyses were not assessed for statistical significance and are descriptive only.

IMmotion151 is a phase III multicenter, randomized, open-label study to evaluate the efficacy and safety of Tecentriq and Avastin versus sunitinib in people with inoperable, locally advanced or metastatic renal cell carcinoma who have not received prior systemic active or experimental therapy. It enrolled 915 people globally who were randomized 1:1 to receive Tecentriq and Avastin, or sunitinib alone.

People in the Tecentriq and Avastin arm received Tecentriq at a fixed dose of 1200 milligrams and Avastin at a dose of 15 milligrams per kilogram via intravenous infusion every 3 weeks until loss of clinical benefit or unacceptable toxicity. People in the sunitinib arm received sunitinib 50 mg orally, once daily for 4 weeks followed by 2 weeks rest until loss of clinical benefit or unacceptable toxicity.

The co-primary endpoints were PFS, as determined by the investigator using Response Evaluation Criteria in Solid Tumors Version 1.1 in people whose tumors expressed PD-L1 (expression ≥1 percent on immune cells), and OS in the overall study population (intention-to-treat).

PD-L1 expression was prospectively assessed using an immunohistochemistry test (SP142) developed by Roche Tissue Diagnostics. Secondary endpoints included OS in people whose tumors expressed PD-L1, PFS as determined by an Independent Review Facility according to RECIST v1.1, investigator-assessed objective response

rate and median duration of response, change from baseline in symptom interference and symptom severity as determined by M.D. Anderson Symptom Inventory, and change from baseline in health-related quality of life as determined by European Quality of Life 5-Dimension Scores.

Stratification factors included the Memorial Sloan-Kettering Cancer Center (Motzer) prognostic scoring system, which predicts for OS based upon an individual's baseline clinical and laboratory characteristics.

Depending on the presence of one or several of five variables, people are classified in one of the three risk groups: "Favorable" with 0 risk factors, "Intermediate" with 1-2 risk factors and "Poor" with ≥ 3 risk factors.

Opdivo plus Yervoy meet PFS endpoint in phase III trial in frontline NSCLC

Bristol-Myers Squibb Company said the ongoing phase III CheckMate-227 study met its co-primary endpoint of progression-free survival with the Opdivo (nivolumab) plus Yervoy (ipilimumab) combination versus chemotherapy in first-line advanced non-small cell lung cancer patients whose tumors have high (≥10 mutations/megabase, mut/mb) tumor mutation burden, regardless of PD-L1 expression.

In the study, TMB was evaluated using Foundation Medicine's analytically validated assay, FoundationOne CDx. Additionally, based on an interim analysis for overall survival, the Data Monitoring Committee recommended that the study continue. The safety profile was consistent with previously reported findings in first-line NSCLC for the combination schedule of Opdivo 3 mg/kg every two weeks and low-dose Yervoy (1 mg/kg) every six weeks.

CheckMate -227 is an open-label phase III trial with more than 2,500 patients randomized across non-squamous and squamous histologies, evaluating Opdivo-based regimens versus platinum-doublet chemotherapy in patients with first-line advanced non-small cell lung cancer. This large program is comprised of three parts: Parts Ia and Ib, and Part II.

Part Ia is evaluating Opdivo plus Yervoy and Opdivo monotherapy versus chemotherapy in patients whose tumors express PD-L1. Part Ib evaluated Opdivo plus Yervoy and Opdivo plus chemotherapy versus chemotherapy in patients whose tumors do not express PD-L1. PD-L1 expression levels were assessed using the Dako-developed diagnostic PD-L1 IHC 28-8 pharmDx.

This announcement is based on an analysis of patients from the Opdivo plus Yervoy arms and chemotherapy arms across all of Part I. There are two co-primary endpoints in Part I for the Opdivo plus Yervoy combination: overall survival in patients whose tumors express PD-L1 (assessed in patients enrolled in Part Ia) and progression-free survival in patients with high tumor mutation burden, regardless of PD-L1 expression (assessed in patients enrolled across Parts Ia and Ib).

Approximately 45% of the TMB-evaluable patients had tumors that expressed high (≥10 mut/mb) TMB in the study. BMS has an ongoing collaboration with Foundation Medicine and will continue the partnership to seek regulatory approval for the FoundationOne CDx as a companion diagnostic to assess TMB for the potential indication of Opdivo plus Yervoy in first-line NSCLC.

Part II is evaluating Opdivo plus chemotherapy versus chemotherapy in a broad population with a primary endpoint of OS. Opdivo and Yervoy are dosed as follows in the study: Opdivo 3 mg/kg every two weeks with low-dose Yervoy (1 mg/kg) every six weeks.

Opdivo is a programmed death-1 immune checkpoint inhibitor that is designed to uniquely harness the body's own immune system to help restore anti-tumor immune response. By harnessing the body's own immune system to fight cancer, Opdivo has become an important treatment option across multiple cancers.

To date, the Opdivo clinical development program has enrolled more than 25,000 patients. The Opdivo trials have contributed to gaining a deeper understanding of the potential role of biomarkers in patient care, particularly regarding how patients may benefit from Opdivo across the continuum of PD-L1 expression.

In July 2014, Opdivo was the first PD-1 immune checkpoint inhibitor to receive regulatory approval anywhere in the world. Opdivo is currently approved in more than 60 countries, including the United States, the European Union and Japan.

In October 2015, the company's Opdivo and Yervoy combination regimen was the first Immuno-Oncology combination to receive regulatory approval for the treatment of metastatic melanoma and is currently approved in more than 50 countries, including the United States and the European Union.

Tyme announces interim phase II data for SM-88 in prostate cancer at ASCO GU Symposium

Tyme Technologies Inc. announced efficacy and safety data from an ongoing phase II trial of SM-88 in patients with non-metastatic, biochemical-recurrent prostate cancer.

Mack Roach III, of the University of California, San Francisco, will present the data in a poster session today at the 2018 American Society of Clinical Oncology Genitourinary Cancers Symposium in San Francisco.

"Prostate cancer patients have limited treatment options and are likely to receive ADT, a hormone therapy that lacks sufficient evidence of efficacy in non-metastatic prostate cancer and may produce considerable toxicities and a reduction in quality of life," said Roach, professor of radiation oncology and urology at UCSF. "Toxicities typically associated with ADT have not been seen with SM-88, which suggest that ADT may be avoided or delayed without progression in patients with non-metastatic prostate cancer. I look forward to continuing to work with Tyme to explore the benefits of SM-88 as an alternative to hormone therapy in prostate cancer patients, particularly those pursuing active surveillance."

Thirteen evaluable patients were assessed from an ongoing phase II trial of SM-88 in nmPC with rising prostate-specific antigen levels, detectable circulating tumor cells and no radiographically detectable metastases. Most patients had previously received ADT after radiation therapy or surgery, but ADT treatment was not permitted during the trial.

Currently, 92 percent of patients (12/13) have maintained radiographic progression-free survival (rPFS) with a median of 12 months since documented biochemical recurrence, and 10 months since starting SM-88 treatment. All 12 patients who have maintained rPFS also exhibited meaningful reductions in circulating tumor cells (CTCs), while the one patient experiencing radiographic progression had a rise in CTCs.

Eighty-five percent (11/13) of patients demonstrated rising or stable testosterone levels, with no drugrelated serious adverse events (grades 3 or 4) observed. According to the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire, all patients reported stable cognitive and sexual function domain measures, including 100 percent (13/13) reporting improved or stable "interest in sex," 62 percent (8/13) reporting no or resolved hot flashes, and 54 percent (7/13) reporting to have "excellent" "overall health" and "quality of life."

DRUGS & TARGETS

FDA approves abiraterone acetate in combination with prednisone for high-risk metastatic castration-sensitive prostate cancer

FDA approved abiraterone acetate (Zytiga) tablets in combination with prednisone for metastatic high-risk castration-sensitive prostate cancer (CSPC). The drug is sponsored by Janssen Biotech Inc.

FDA initially approved abiraterone acetate with prednisone in 2011 for patients with metastatic castration-resistant prostate cancer (CRPC) who had received prior chemotherapy, and expanded the indication in 2012 for patients with metastatic CRPC.

The latest approval was based on LATITUDE (NCT01715285), a placebo controlled international clinical trial that randomized 1,199 patients with metastatic high-risk CSPC. Patients received either abiraterone acetate, 1,000 mg orally once daily with prednisone 5 mg once daily (n=597), or placebos orally once daily (n=602). Patients in both arms received a gonadotropin releasing hormone or had a bilateral orchiectomy. The major efficacy endpoint was overall survival (OS). Median OS was not estimable and 34.7 months in the abiraterone acetate and placebos arms, respectively (HR 0.621; 95% CI: 0.509, 0.756; p<0.0001). The median time-to-initiation of chemotherapy was not reached for patients on abiraterone acetate with prednisone and 38.9 months for those receiving placebos (HR 0.44; 95% CI: 0.35, 0.56; p<0.0001).

The most common adverse reactions in at least 5% of patients receiving abiraterone acetate on LATITUDE were hypertension, hot flush, hypokalemia, increased alanine aminotransferase or aspartate aminotransferase, headache, urinary tract infection, upper respiratory tract infection, and cough.

The recommended dose for Zytiga for metastatic CSPC is 1,000 mg orally once daily with prednisone 5 mg orally once daily. Patients receiving ZYTIGA should also receive a gonadotropin-releasing hormone (GnRH) analog concurrently or should have had bilateral orchiectomy.

Full prescribing information is available here.

FDA granted priority review for this application and it was approved more than a month ahead of the due date.

Foundation Medicine and EORTC collaborate comprehensive genomic profiling

Foundation Medicine Inc. and the European Organisation for Research and Treatment of Cancer announced a collaboration in which Foundation Medicine's comprehensive genomic profiling tests will be used to inform patient eligibility for oncology clinical trials through the EORTC's Screening Patients for Efficient Clinical Trial Access program, which is a pan-European network built by the EORTC with key institutions collaborating to provide efficient access for patients to molecularly driven clinical trials.

Under the agreement, Foundation Medicine will provide genomic testing services for the SPECTA program through three of its genomic profiling assays: FoundationOne, its flagship assay for solid tumor cancers that includes analysis of genomic biomarkers such as microsatellite instability and tumor mutational burden, FoundationOne Heme, an assay for hematologic malignancies and sarcomas that also includes MSI analysis, and FoundationACT, a liquid biopsy assay for solid tumors.

Samples will be processed at any one of Foundation Medicine's laboratories located in the United States and Europe.

Abbott PathVysion HER-2 DNA Probe assay to be used in ANGLE study

ANGLE plc has signed an agreement with Abbott in which Abbott will supply ANGLE with its proprietary PathVysion HER-2 DNA FISH Probe kits for ANGLE's ANG-002 FDA study for FISH (fluorescence in situ hybridization) analysis of circulating tumor cells in the form of a research grant.

FISH analysis, which is a form of investigation of the cancer cells used with solid tissue biopsy to help select treatment, is one of the exploratory endpoints for ANGLE's FDA study in metastatic breast cancer.

The objective of this endpoint is to demonstrate that CTCs can be harvested from the blood of metastatic breast cancer patients using the Parsortix system and that the harvested CTCs can then be subjected to FISH analysis to determine their HER-2 status.

PathVysion determines HER-2 gene status, identifying which patients are HER-2 positive. A positive PathVysion HER-2 result in Parsortix harvested CTCs would demonstrate feasibility of evaluating use of the assay in a breast cancer liquid biopsy in metastatic breast cancer patients.