Remarks* by

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Thank you for that kind introduction and thanks for your terrific leadership of ASCO at this important juncture in cancer research. Thank you to the American Society of Clinical Oncology and it's nearly 45,000 members. Your commitment to cancer research and care has led to meaningful progress for our patients.

A few weeks ago, I appeared before the Senate Appropriations subcommittee that funds the NIH. The Chair of that subcommittee, Senator Roy Blunt, asked me about the future of cancer research. I explained that this is a time of great hope and optimism. We have seen real therapeutic progress with kinase inhibitors, immunotherapy, and precision medicine and the ASCO community is a huge part of these advances. As I told Senator Blunt, the day the ASCO Abstracts are finally released online is like Christmas morning to me.

I have to confess, I originally joined the American Society of Clinical Oncology in 1998 in response to one of the most primal of human emotions—abject fear. Let me explain. You see, back then, I was an oncology fellow at the Dana-Farber/Partners Cancer Care. I was barely done with residency and I was called upon to provide care for some sick and often desperate patients. In some cases, they had made grueling trips to Boston, traveling hours to see a cutting-edge specialist at Harvard. And, often, the first doctor they ended up seeing was me.

As a new cancer doctor, I did not feel up to the task. I suffered from that "imposter syndrome" that most young doctors feel. Medical residency had not prepared me for this. I felt afraid of making a mistake, of missing something important, and of letting these people down.

So, I joined ASCO, probably for the same reason as many of you: from a desire to become better educated about cancer so I could take better care of my patients. Then, as now, ASCO provided educational materials for oncologists, the most important of which, to me, was the Journal of Clinical Oncology (JCO). As an oncologist-in-training, I felt that if I read every

*This text is the basis of Dr. Sharpless's oral remarks. Use with the understanding that some material may have been added or omitted during final presentation.

issue of the JCO as it came out, I would be sufficiently knowledgeable about cancer to be able to help my patients.

Back in that pre-Internet era, we used to pass around and carry with us these Xeroxed copies of articles. We employed these as a totem to ward off our clinical insecurities. If we were battling cancer, JCO was provisioning the armor.

I recall carrying around a raggedy-eared copy of a 1990's Art Skarin paper from the JCO, that I would quickly scan before seeing a new patient with lung cancer. I recall learning how to use tamoxifen to treat ER positive breast cancer from Hy Muss, also via his writing in the JCO, many years before I actually met Dr. Muss.

Reading the JCO would help me and my peers march into the exam room of a new patient suffering from a cancer we had not treated before. In those rooms waited for us some extreme challenges, and I can still picture their faces: the mother of four with metastatic breast cancer; the incarcerated young sarcoma patient who left prison once a week so I could give him chemo; the guy with a metastatic islet cell tumor, whose main symptom was that he kept passing out at work from severe hypoglycemia; the young HIV positive artist with lymphoma, whose tumor we cured, but whose outcome was still terrible because of his failing immunity.

These patients were suffering and wanted help. They needed a really, really good oncologist: someone who was educated and thoughtful. So, I joined ASCO in 1998 so that I could become that—a really good oncologist, whose education, in large part, developed from reading the JCO.

Besides the JCO, another of ASCO's most important tools is happening right here and now—the ASCO Annual Meeting, which is one of the most important events for cancer doctors, patients, and other caregivers around the world.

I am happy to share the news, as you may have seen in last week's Annual Report to the Nation on the Status of Cancer, that we continue to see a steady decline in cancer mortality. In 1991, the cancer mortality rate was 215 deaths per 100,000 people in the US. In 2015, that number was down to 159. There is reason to believe that the number is even lower now and will continue to decline. This represents decreases in cancer death for men, women, and children, and for all major ethnic groups.

More good news is the strong, bipartisan support we're receiving from Congress. For the 4th year in a row, we have seen budget increases for NIH and NCI. The fiscal year 2018 Omnibus spending bill passed in March provides a $275 million increase to the NCI budget, as well as continued full funding for the Cancer Moonshot. So, with new discoveries, successful treatment approaches, continued research progress, and additional funding, as a community, oncologists can feel a lot of optimism. The potential for breakthroughs has never been greater than it is right now.

That's the good news—and it is good news. But, no doubt, we still face significant challenges. These are well known to this audience: little progress in certain cancer types such as

pancreatic adenocarcinoma and glioblastoma. There are still too many children dying of cancer. We have to admit that it is not sufficient to make progress in just the common cancers or the best-understood cancers or the easiest-to-treat cancers. NCI is charged with making progress in *all* types of cancer to benefit *all* patients. Even when we can cure kids and adults of cancer, too often this comes with the cost of significant and lifelong toxicities from the cure.

One side effect of curative therapy, the true consequences of which we are just starting to fully appreciate, is financial toxicity, which can be devastating for cancer survivors. I would argue these areas of continued slow progress in turn reflect an incomplete understanding of cancer biology, and challenges to the ways we do cancer research.

I think it is NCI's job to take these challenges head-on. When I started in this new role last October, I decided to take 6 months to go on a "listening and learning tour." During that time, I spoke to many patients, advocates, clinicians, and scientists about what NCI does well and areas that needs improvement.

That effort helped me identify four key focus areas on which I wanted to focus as leader of NCI. These are not new areas for NCI. However, they are areas where I think the scale and reach of NCI plays an especially important role and NCI's resources, convening power, and leadership can act as catalysts.

They are Basic Science, Workforce Development, Big Data, and Clinical Trials. You can read more about each of these areas on my blog on cancer.gov, but I will share some highlights that I think will be of greatest interest to ASCO attendees.

I don't think the basic science work of cancer is done. NCI continues to strongly support investigator-driven basic research and always will while I am director. We have a much better understanding of cancer now than at any time in human history, but we must also admit that we need more fundamental research in this area. I believe a top-down approach is not the way to go here. Focus has to be on investigator-initiated discovery. NCI has some role to identify topics for specific focus and once we have done that, we have to sit back and let the proverbial magic happen.

One of the best ways to support investigator-initiated science is through the funding of the Research Project Grants—the RPG pool. This pool funds the vast majority of investigator-initiated awards—the R01s and the even larger program project grants, such as P01s. Toward that end, this year I have dedicated an additional $127 million to investigator-initiated science. This is the largest increase to the RPG pool since 2003 and is possible thanks to significant increases in our congressionally appropriated budget over the past few years. While this is not solely for basic science, this is the most straightforward way to assure we continue to fund investigator-initiated basic science. Discoveries in basic science propel progress for patients.

One of our most important jobs at NCI—perhaps the most important job of NCI—is to ensure a talented and innovative research workforce for the decades ahead. We must continue to press for a diverse workforce in terms of background, interest areas, ethnicity, and gender. We must broaden our notions of who we consider to be our colleagues. For example, I predict we

will be working more closely with an increasing diversity of experts: immunobiologists, computer engineers, healthcare economists, geriatricians, data scientists, and yes, community oncologists.

We are doing many things in this area, but one, in particular, is intended to address the plight of the Early Stage Investigator, or ESI. Again, thanks to the support of Congress, this year NCI is able to set aside dedicated funding for ESIs to increase their chances of getting a first major grant (an R01) from NCI. This extra funding will increase the number of first R01s to ESIs by at least 25%.

NCI will also be looking at many strategies to encourage development of the right skill sets for the future of cancer research through dedicated funding of training grants and professional development opportunities.

Big Data is another area where we've seen a transformation that creates great opportunities for cancer research and care, but also new challenges. Embracing the potential of big data will add speed and dimension to our work across the cancer enterprise. Consider that more than 90% of all digital data created to date across all fields was produced in the last 2 years.

You hear a lot about data sharing and that is important. But, we must also move beyond passive data sharing to intentional data aggregation in order to fully leverage the power of data, establishing linkages and interoperability of diverse, complex data sets to understand cancer care and provide real world evidence. For example, linking genomic data with pathology data with radiology data with clinical data mined by machine learning from EHRs in a large number of patients, while assuring data privacy and security. The power of that is incredible. This will benefit the entire research community, including all of you. Research questions that are almost intractable by traditional means can be addressed by large, annotated, multimodal datasets.

So, how are we going to harness big data? This is a place where we need to pay attention to the workforce, attracting young data scientists into cancer research. We will focus on the linkage of many large datasets maintained by NCI to provide interoperability. There are several interesting efforts in this area to talk about. For example, we are going to link the enormous data set of the cancer genome atlas, where possible, to the clinical data for those patients.

NCI's Surveillance, Epidemiology, and End Results (SEER) program is one of the biggest of NCI's big data initiatives, and is taking some innovative steps worth noting. The NCI-supported SEER program was created by federal law in 1971 as part of the National Cancer Act. It has collected statistics on cancer deaths and outcomes for 45 years to support research on the diagnosis, treatment,c and outcomes of cancer since 1973. It consists of 16 population-based registries covering 33% of the US population. These registries collect information on all cancer cases for residents of the state or region. They represent racial and ethnic minorities and various geographic subgroups.

SEER is one of the most important things NCI does to support population sciences research. The SEER contracts were just re-competed and we are actively exploring approaches to innovatively augment this rich dataset's capabilities through many sorts of novel data linkages.

Beyond SEER, we are also working on data initiatives with federal partners like the Department of Energy, which gives NCI access to cutting-edge, exascale computing, as well as with the FDA and CMS, which have interesting, large datasets of potential value to cancer researchers. These data efforts are supported by a developing NCI Cancer Data Ecosystem, which is being significantly amplified with new targeted funding from the Cancer Moonshot. This includes highly successful cloud resources for storage and computing, as well as robust efforts for NCI to set standards for data sharing and interoperability.

We have to do these things because the costs of not harnessing big data are too great. By doing this, we can learn from every patient.

Every one of today's standard-of-care therapies is available because of a past successful clinical trial, but translating today's discoveries into routine, effective treatments isn't a matter of doing more of the same.

There are several problems that we have to face: decreased accrual and poor accrual of underrepresented populations; increasing per-patient costs; spiraling times to open and to the completion of clinical trials. These problems are bad for clinical researchers, and even worse for patients.

As a major funder of clinical trials, NCI can improve these problems. We have to get rid of unnecessary exclusion criteria and confusing consent forms. We need to encourage and expand the use of central IRBs. We need trials with innovative, adaptive designs to identify inactive agents quickly and thereby prioritize good drugs for further testing. We need trials that are based on a modern understanding of cancer.

The fact of cancer's tremendous heterogeneity means that traditional clinical trials models are becoming less useful. Largely gone are the days when the cardiology paradigm of clinical trials reigned when we enrolled enormous numbers of patients into large Phase III trials with slightly different treatment protocols, where very modest improvements upon a largely ineffective regimen was considered success.

One emerging approach about which I am excited is demonstrated by the NCI-MATCH trial. NCI-MATCH is an example of innovative trial design. This precision oncology trial allocated patients to one of approximately 30 arms of therapy based on somatic genetic testing.

Some of the first efficacy results from MATCH are being presented here at ASCO, so I won't go into detail, but I would like to highlight the importance of this trial as an example of new ways to conduct clinical research. This map shows, what to me, is one of the most important facts of MATCH. Coordinated with ECOG-ACRIN, it has enrolled more than 6,000 patients to cutting-edge therapeutic trials at 1,100 sites across the country. It has been the fastest accruing trial in NCI's history. This shows us that even highly complex precision medicine trials can be conducted in the ethnically diverse communities where real-world patients live. If we have well-designed efforts like MATCH, the patients will come.

We are also employing this same approach through the Pediatric MATCH Trial. Working with the Children's Oncology Group, NCI has brought Pediatric MATCH to 200 sites across the country with eight arms currently open. These efforts are important and will become even more so as more and more drugs are approved based on driver mutation rather than on tissue-of-origin.

Mark my words, trials like MATCH and Pediatric MATCH are already changing how we make progress in oncology.

Lastly, while novel trial designs like that of MATCH are generating much excitement, larger, traditionally structured trials to define standards of care remain critical for progress in cancer research, and NCI will continue its robust support for these efforts. For example, at this meeting, results from the TAILORx trial will be reported. This clinical trial in 6,700 women with breast cancer has examined the use of antihormonal versus cytotoxic therapy for women with ER positive breast cancer based on results of an RNA-based genetic risk score. The results of this trial will have implications for thousands of women with breast cancer over the next few years.

NCI's major efforts with regard to large clinical trials are largely supported through our clinical trials networks like the National Clinical Trials Network (NCTN). One of the major challenges for these networks over the past few years, however, has been a rapid increase in the per-patient costs for patients on trials. NCI appreciates the problems that these skyrocketing costs have caused for NCTN trials, and today I am announcing that we are going to help.

I am announcing that, this year, we will be providing an additional $10 million to support trials run within the NCTN and NCORP. The majority of this funding will be used to augment per-patient reimbursement rates at 180 sites that treat adult or pediatric cancers.

I'm sure we will hear about rapid progress in clinical oncology research at this meeting. What we are doing together is shaping the future of cancer research and changing lives. Before I conclude, and we dive into all that is ASCO—the posters, the sessions and the networking—I'd like to talk about something that's been on my mind.

An almost overarching worry of the cancer doctor today has become the management of expectations: we don't want to overpromise and give people—especially patients—false hope, but I am worried we have been losing the point. I think we have become scared to tell our patients that we hope to "cure" them and it may be time to re-examine how we communicate our efforts in this area.

As an oncologist, I used to cringe at the notion of "curing cancer" when talking to patients. What if I told them they were cured, but then the cancer actually came back? I especially know why the notion of "cure" makes so many of us uncomfortable. Curing cancer, making it go away and never come back, is really hard—much harder than initially conceived—and the word "cure" should not be thrown around lightly with vulnerable patients present.

It is also worth making two points. First, we *are* curing patients now, and more people than ever—even some people with really bad cancers at very advanced stages. I never thought I'd see some of the results that we are now seeing in metastatic lung cancer and melanoma.

Second, even if the idea of curing cancer makes us uncomfortable, it is what our patients and our funders expect. They don't just want extended progression-free survival or enhanced quality of life or reduced costs or whatever other surrogate marker we might pick.

They expect us to deliver.

This was the subtext behind Senator Blunt's question to me when I recently testified. Our patients and their representatives want to know that we are making progress to prevent and to cure this set of formidable diseases.

After being a member of ASCO for 20 years, I'm happy to say that those early fears of walking into a new patient's room and having absolutely no options are going away if not already gone.

Almost every day we learn of new discoveries, advances and approaches that show promise. We have options. We have treatments. And sometimes, we do have a cure. Now, there is enormous optimism in our field. There is reason for this optimism.

Thank you.