Hello everyone, my name is Shaily Arora and I am an acting associate director for Safety in the Office of Oncologic Diseases at the FDA.

I would like to welcome you to our introductory video ahead of our workshop on February 2nd and 3rd titled Barriers and Solutions to Oral Anticancer Agent Adherence.

This FDA oncology workshop has been designed to explore the issues surrounding patient non-adherence to oral anticancer medications, to find out the current gaps in knowledge, to discuss possible solutions, as well as identifying the future research questions.

FDA has co-sponsored this workshop with American Society for Clinical Oncology and my co-chair for this workshop is Dr. Donald Harvey and in this video we would like to briefly describe the rationale behind organizing this workshop, discuss overarching goals and introduce the agenda for the upcoming meeting.

Now before I talk about this workshop, I just want to take a couple of minutes to introduce the term medication adherence. Medication Adherence is defined as the extent to which patients take medications as prescribed by their health care providers. It is a behavioral process that is influenced by many factors including complexity of the drug regimens, adverse event profiles, patient specific factors, as well as social and economic reasons.

In the last decade, especially the last few years, there has been a dramatic rise in the number of oral anticancer agents that have become available and my co-chair Dr. Harvey is going to share some data with us shortly about that. Despite the effectiveness of these oral agents in cancer patients, nonadherence to oral anticancer treatments is common with some studies reporting average adherence rates as low as 40%. This represents a growing challenge, due to the paradigm shift in anti-cancer treatment from parenteral chemotherapy to oral anti-cancer medications. Studies done in several malignancies have shown that nonadherence can negatively impact treatment response, survival and quality of life. There is a common assumption that given the severity of cancer and the disease state, adherence to these oral anticancer agents would be higher, but that has not been the case.

The problem of nonadherence is now widely recognized and this FDA-ASCO workshop will provide an opportunity for experts and leaders from industry, academia, regulatory government agencies, patient representatives, and healthcare providers to discuss the implications of non-adherence, delve into steps that can be taken during the drug development process that may potentially improve adherence and talk about common barriers and offer potential solutions to medication nonadherence . Our goal with this workshop is to increase the cancer care community's knowledge about the barriers and offer potential solutions to oral anticancer agent adherence.

3:25 With that I would like to invite Dr. Donald Harvey to introduce himself as well as provide a brief background, describe the structure of our workshop and the agenda.

Don:

3:37

Thank You Shaily. So I am Don Harvey. I am a Professor or Hematology/Medical Oncology here at Emory University and Director of the Phase 1 Clinical Trials Program. Probably most importantly, I am a pharmacist so thinking about adherence to oral medications within cancer, as we try to turn cancer into a chronic disease.

The oral route is going to be pivotal to trying to do that successfully. With that comes freedom for patients: from infusions, freedom from treatment centers. But also a number of challenges of helping patients get drugs and be adherent to them overall.

As you look back at the history at the FDA approval of new molecular entities from 2006-2010, there are only about 5-10 new molecular entities approved for the treatment of cancer. But since that timeframe, and particularly over the last 5 years, we have had no less than 40-50 new molecular entities approved in various diseases and various ways for the treatment of cancer. With that comes a lot of potential

challenges for patient adherence including: drug interactions with food, drug interactions with antacids, as well as unique schedules to () that might be different from other chronic medications that patients may take. And we also have to remember that patients with cancer often have comorbidities, so we are adding oral therapies to their already existing medication regimen for diseases such as hypertension, diabetes, and others.

And so, with that, I firmly believe that adherence to medication in cancer begins at the earliest phase of development. The medicinal chemistry level, the formulation level, how we give drugs, whether it be with food or without, how patients tolerate those drugs, how we manage their adverse events, really all comes from very earliest first in human trials. Identifying the dose that treats the cancer, but most importantly, is tolerable, continues to be the primary focus of our work in early phase trials.

So, with that, the first day of the agenda for this workshop is going to focus on that drug development aspect and clinical pharmacology. How can we leverage the tools that we have now to improve the ability of patients to be adherent to drugs, to manage adverse events, to try to understand what the therapeutic window is such that we don't have to reach toxic doses of drug that patients may not tolerate for the long term.

The second session is going to focus more on trial design and data output from early phase and subsequent phase studies, which gives us understanding what adverse events look like, how we can manage them, and move forward more easily. Just as importantly, what the adherence rate within a given trial population is. Because if the adherence rate isn't optimal in a trial population, it is likely only to go down when the drug is marketed subsequently. So understanding that rate of adherence within that population is critical to beginning the concept of helping patients be as adherent as possible to their medication when used alone or in combination.

With that, I'll turn it over to you Shaily for further description of the agenda.

6:42 Thank you, Don, for such a great description of Day 1 for our workshop.

Given that adherence is a behavioral process, which is influenced by drug as well as patient specific factors, we have dedicated the second day of our FDA-ASCO workshop to focus on social and economic reasons as well as patient specific factors, that impact adherence.

We will begin Day 2 of the workshop by focusing on the Social Determinants of Adherence. During this session we will engage in a conversations with our patient representatives, and healthcare providers from several clinical practice settings to

better understand the impact of Health Economics such as co-pays and coverage policies on medication adherence. We will also explore the impact of Patient and health care provider relationships, patient specific characteristics such as literacy, language barriers as well as community characteristics for e.g., lack of access to transportation, not having a social support system, prior exposure to discrimination or stigma and how all of those may play a part in nonadherence.

The second and third sessions on Day 2 will look at Adherence in Special Populations with one session dedicated to Adolescent and Young Adults and another for Older Adults. During these sessions our esteemed panelist would discuss patient-specific concerns for each of these populations and how they may have an impact on medication adherence along with offering some potential solution.

We truly have designed this workshop to cover a breadth of issues impacting non-adherence to oral anticancer medications. I hope this video was able to provide a brief glimpse into our upcoming workshop which will facilitate a discussion of the limitations of the current drug development approaches including clinical trial designs, methodologies to accurately capture adherence, and strategies to improve our knowledge of the complexity of these regimens, and look patient specific factors that act as barriers to adherence.

I want to take this opportunity to thank everyone for listening and invite you to join us on February 2nd and 3rd as we,

together, explore the Barriers and Solutions to Oral Anticancer Agent Adherence.

Thank you and see you on February 2nd.