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EDITED TRANSCRIPT

PFE.N - Pfizer Pflash: A Spotlight on the PF'4404 (SSGJ-707 / PF-08634404) Clinical Development Strategy

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OVERVIEW:

Company Summary

REFINITIV

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PRESENTATION

Operator

Good day, everyone, and welcome to Pfizer Pflash, a Spotlight on the PD-1 x VEGF Bispecific PF'4404 Clinical Development Strategy.

Today's call is being recorded.

At this time I would like to turn the call over to Francesca DeMartino, Chief Investor Relations Officer and Senior Vice President. Please go ahead, ma'am.

Francesca DeMartino - *Pfizer Inc - Chief Investor Relations Officer, Senior Vice President*

Thank you and good morning everyone. I'm Francesca DeMartino, Chief Investor Relations Officer. On behalf of the Pfizer team, thank you for joining us for the latest episode in our Pflash series. Today's call will be recorded and available for replay on our IR website, Pfizer.com.

As a reminder, our Pfizer Pflash series is intended to serve as an educational deep dive into our pipeline, products, and people. Each call will spotlight a specific product, therapeutic area, or growth initiative and give you an opportunity to hear from and interact with our business leaders. Today's session will begin with a conversation followed by a live Q&A. As a reminder, this call is intended only for the investment community, including our sell side analysts and institutional investors. If you are unable to join the entirety of the event, you can find the replay available on our website.

I want to note that on today's call we will be making forward-looking statements. I encourage you to view slide 2, in our presentation and the disclosures in our SEC filings, all of which are available on our website at pfizer.com.

Forward-looking statements on the call are subject to substantial risks and uncertainties, speak only as of the call's original date, and we undertake no obligation to update or revise any of the statements. With that, let's get started.

Oncology is a key area of focus for Pfizer. In July of this year, we closed a licensing deal with 3SBio for global ex-China rights to the bispecific antibody SSGJ-707, which will, which we will now refer to as PF''4404 or just '4404.

In our last Pfizer Pflash, we provided an introduction to '4404 and promised to share an update on our clinical development plans. Today we'll expand on that development strategy which we believe has the potential to establish '4404 as a backbone therapy across multiple tumor types.

Before we kick off the main discussion, I'd like to take a moment to introduce our speaker, Jeff Legos, Pfizer's Chief Oncology Officer. In addition, Johanna Bendell, Chief Development Officer for Oncology; and Arati Rao, '4404 Franchise Head, will participate in our Q&A. Jeff, Johanna, and Arati, welcome and thank you so much for joining the conversation today.

Jeff, let's get started. Can you remind us what '4404 is, how it works, and how it fits into Pfizer's broader oncology pipeline and portfolio?

Jeff Legos - *Pfizer Inc - Chief Oncology Officer*

Thanks, Francesca. Yes, I'm very happy to. '4404 is a bispecific with potential transformative mechanism of action that may enable it to be a foundational therapy across multiple cancers. As shown on the left hand side of the slide at the heart of '4404 is its ability to target both PD1 and VEGF. PD1 is a key receptor that typically acts to prevent immune cells from attacking cancerous cells. VEGF, the other target of '4404, plays an important role in tumor blood vessel formation.

We've seen that PD1 and PDL1 checkpoint inhibitors are amongst the most broadly impactful oncology medicines developed to date. Furthermore, emerging internal Phase 3, data has shown that the combination of PD1 and VEGF inhibition in a single molecule like '4404 has the potential to achieve superior efficacy versus PD1 inhibition alone.

If these initial data achieved with PD1 and VEGF mechanism of action can be proven out in global Phase 3 studies and in additional treatment settings and tumor types alongside an accepted safety profile, these results can truly be transformational for patients with cancer.

Next please. We believe that '4404 is a foundational asset and a strong, seamless bet with Pfizer's oncology strategy. First, many of the types where PD-1 x VEGF specific may have significant impact are aligned with our established disease areas of focus. These include thoracic, genitourinary, and gastrointestinal cancers.

Second, '4404 is a multi-specific antibody, one of our three core modalities where we have deep experience and industry leading capabilities. And third, there's an opportunity to explore combinations with our industry leading ADC portfolio, including the vedotin class of ADCs, where a growing body of clinical data show potential synergy with anti-PD1 agents.

This strategic alignment is critical for our goal to develop '4404 into the leading PD1x VEGF bispecific and establish it as a backbone therapy across multiple tumor types. We're laser focused on developing '4404 with speed, with breadth and depth. Speed is facilitated by our robust global development capabilities, with seven new clinical trial initiations with '4404 expected in the near term.

As the first of many planned waves within our development strategy, breath leverages presence in multiple key disease areas where PD1 and VEGF specific may have significant impact and underpins our plans to develop '4404 multiple tumor types. Depth is driven by our unique blend of capabilities, focus, and modalities to develop '4404 across multiple treatment settings, lines of therapy, and in novel combinations within a given disease.

Francesca DeMartino - *Pfizer Inc - Chief Investor Relations Officer, Senior Vice President*

Thanks Jeff. Let's double click on capabilities and presence. Can you elaborate how you see those contributing to Pfizer's Dalton of '4404?

Jeff Legos - *Pfizer Inc - Chief Oncology Officer*

Certainly, go to the next slide, please. Pfizer has many capabilities that leave us well positioned to create value with '4404, which we view as a foundational asset. A key part of our potentially differentiated '4404 strategy is the speed at which we can move in clinical development. For oncology, speed is not just the pace of work, it's about working smarter, leveraging our global scale, and harnessing technology to enhance efficiency and innovation.

We work smarter as an organization because of our team. Across our clinical and medical organizations, we have more than 50 medical oncologists who bring unparalleled experience and are empowered to make decisions and move quickly. These leaders, together with our understanding of regulatory and operations teams, make Pfizer an industry leader in innovative clinical design and regulatory strategies that bring potential new therapies to patients with cancer.

Our global scale and clinical operations and supply provide us with the agility and global clinical development. In addition to our global clinical footprint, we have 10 manufacturing and clinical trial supply sites on three continents, including four in the United States. These networks and colleagues allow us to execute our clinical development plans nimbly and with the highest quality.

Highlighting our unprecedented speed, here are a few of the many achievements which we have made in the last 3-months-plus since closing the licensing deal.

First, we've submitted five new IMDs with the FDA. We've worked diligently to select over 500 global clinical trial sites for our '4404 studies in more than 25 countries. And finally, we've accelerated timelines for tech transfer and have successfully manufactured '4404 drug product here in the United States.

Francesca DeMartino - *Pfizer Inc - Chief Investor Relations Officer, Senior Vice President*

Thanks Jeff. Let's bring some of those concepts together and talk about the near term plans for '4404's clinical development.

Jeff Legos - *Pfizer Inc - Chief Oncology Officer*

Absolutely. Let's move to slide 7, please.

Here we show our first wave of planned near term clinical trials, starting with our Phase 3, pivotal studies. These will be the first Pfizer sponsored studies for '4404. Already on ClinicalTrials.gov. These include a study in frontline non-small cell lung cancer, including both squamous and non-squamous histologies, and one in frontline metastatic colorectal cancer.

Beyond these pivotal trials, we plan to initiate 5 additional studies with near term starts in lung cancer. These include a Phase 1, Phase 2 study to evaluate '4404 in combination, including with some of our ADCs, as well as a Phase 2, Phase 3 study in frontline extensive small cell lung cancer.

In GI, we plan to initiate a Phase 1, Phase 2 study in hepatocellular carcinoma, and in GU we have two planned Phase 1, phase 2 studies one evaluating '4404 in locally advanced or metastatic urothelial carcinoma, and the second one in locally advanced or metastatic renal cell carcinoma.

Importantly, these seven anticipated near term study starts are only the beginning of our plans for '4404. We're actively working through a second wave of potential development opportunities that could deal trial starts for another 10 additional indications and 10 or more novel combinations before the end of 2026. Which is a good segue to how we're thinking about our depth of development across settings, across lines of therapies, including novel combinations. Next slide, please.

We're aiming to make '4404 a key part of our future oncology arsenal by displacing the current standard of care PD-1 and PDL-1 and VEGF agents with the new PD-1 x VEGF bispecific backbone therapy across multiple tumor types.

In parallel, we plan to look across lines of systemic therapy to potentially establish a new generation of chemotherapy sparing regimens by a combinations of '4404 with potentially synergistic antibiotic drug conjugates, and we plan to look at opportunities to expand '4404's reach to impact patients even earlier in their treatment journeys, such as in the neo-adjuvant and adjuvant settings.

Francesca DeMartino - *Pfizer Inc - Chief Investor Relations Officer, Senior Vice President*

So Jeff, on the planned Phase 3, program design, how is Pfizer engaged with health authorities and how have those discussions shaped the path forward?

Jeff Legos - *Pfizer Inc - Chief Oncology Officer*

It's an excellent question. Let's move to slide tab 10, please. We've been very thoughtful in our engagement with health authorities and have relied on our global Phase 3, studies in non-small cell lung cancer and metastatic colorectal cancer. The goal of these discussions was to establish a framework through which we can position the '4404 development franchise to move with both maximum rigor and speed.

Included in this framework are 4 core principles that we believe are consistent with the evolving health authority expectations and that may serve as a template for future '4404 pivotal trials. Firstly, we'll make overall survival a primary endpoint, either alone or a dual primary with progression-free survival.

Secondly, we'll include at least 20% enrollment of US participants and appropriately diversify outside of that to achieve representation of our global patient population. Third, our Phase 3, programs will be enabled by a robust dose optimization studies in line with the US FDA's Project Optimus.

And lastly, we'll look to engage the FDA and global health authorities for pre-phase 3, advice to inform optimal trial design and execution. While these may seem straightforward, their effective and efficient implementation has the potential to meaningfully differentiate the speed and success of our clinical trials both in the near term and beyond.

Francesca DeMartino - *Pfizer Inc - Chief Investor Relations Officer, Senior Vice President*

Great. Let's now transition to the '4404 clinical data starting with lung cancer. Lung cancer remains a significant unmet medical need, but not all lung cancer is the same. Can you discuss the opportunity for new therapies and the broader market segmentation?

Jeff Legos - *Pfizer Inc - Chief Oncology Officer*

Sure, if we can move the slide as well please. Let me start with some of the epidemiology. Lung cancer continues to pose a significant global health burden, with over 2.7 million new diagnoses expected globally for 2025. In the United States alone. This includes approximately 315,000 incident and newly recurrent cases.

Despite a decade of declining death rates, the 5-year survival across ages is 32% for non-small cell lung cancer and only 9% for small cell lung cancer. This underscores the urgent need for continued innovation in early detection and treatment strategies across lung cancer, a large and growing market that's expected to be approximately $70 billion by 2030.

On slide 13, this shows the segmentation of lung cancer, highlighting that this tumor type is not a single disease, but rather a collection of multiple molecularly distinct diseases. This segmentation helps to stratify patients and is the foundation of precision therapy selection.

The two primary histologic subtypes are non-small cell lung cancer, which makes up approximately 85% of the cases, and small cell lung cancer, accounting for the remaining 15%. Non-small cell lung cancer is further divided into distinct subtypes squamous and non-squamous histology, with the non-squamous population being roughly threefold larger than squamous. Historically, the squamous cell histology has been more difficult to effectively treat.

Additionally, PDL1 expression has become a critical biomarker for guiding immunotherapy decisions in non-small cell lung cancer. This is typically determined through what is called tumor proportion score or TPS, which measures the fraction of cancer cells in a tumor that expressed PDL1. Historically, higher TPS scores have been shown to predict better outcomes with immune checkpoint inhibitors. TPS scores greater than 1% are

categorized as PDL1 positive, accounting for approximately two-thirds of cases, and a TPS score of less than 1% are categorized as PDL1 negative, accounting for the remaining one-third.

Within the non-squamous, non-small cell lung cancer, there's another tool to help define distinct molecular subtypes. This looks at the genetic drivers of cancer bucketed into the actionable genomic alterations, including EGFR, ALK, BRAFV600, and KRAS. The presence of these mutations often prioritizes targeted small molecule therapies over immunotherapy as the first line of treatment.

Francesca DeMartino - *Pfizer Inc - Chief Investor Relations Officer, Senior Vice President*

That's really helpful context, Jeff. Thank you. So data for '4404 plus chemotherapy and non-small cell lung cancer were recently presented at the Society for Immunotherapy of Cancer meeting, or SITC. Can you share the highlights of that presentation?

Jeff Legos - *Pfizer Inc - Chief Oncology Officer*

If we can move to slide 14, please. Last week's presentation at SITC was from an open label randomized Phase 2, trial of '4404 in combination with chemotherapy as the first line treatment in advanced non-small cell lung cancer.

This study is being conducted in China by 3S Bio and was designed to evaluate the safety, tolerability, and anti-tumor activity of '4404 in combination with chemotherapy. This was a head to head trial with the standard of keratisillizumab, an anti-P1 and leading approved agent in China, in combination with chemotherapy.

Patients of both histologies were enrolled irrespective of PDL1 TPS score. Part one was a chemotherapy combination with a dose escalation of '4404 in patients with non-squamous tumors versus tislelizumab plus chemo combination one. Part two was a similar design for patients with squamous disease and included both a dose escalation cohort A and a dose expansion cohort B. The 10-mg per kilogram dose was selected for cohort B.

The efficacy data from non-squamous, non-small cell lung cancer patients are shown on slide 15, and are suggestive of deep and durable responses with a firm objective response rate that was numerically higher for '4404 in combination with chemotherapy across both dose levels.

As shown in the left panel, the confirmed objective response rate for '4404 plus chemotherapy was 50% at the 5-mg per kilogram dose and approaching 60% for the 10-mg per kilogram dose compared to 40% for the tisillizumab combination therapy.

The depth and durability of response for patients receiving '4404 at the 10-mg per kilogram dose is shown on the spider plot on the right. Each line represents an individual patient and shows tumor shrinkage from baseline, where the lines going down are good. In addition, you can see that many of the lines continue to further deepen and stay there, reflecting a deepening of this response over time and providing an early glimpse of the response therapy.

We're particularly encouraged by the efficacy for the 10 mg per kilogram dose group, which has informed the planned phase 3, pivotal start and will also be the focus of today's discussion around these phase two results.

On slide 16, are the efficacy data in the squamous histology group. Let's put cohort A in the top panel. The results for patients receiving '4404 at the 10-mg per kilogram dose are suggestive of double responses independent of PDL1 expression. The depth of response is shown in the waterfall plot in the left panel. These plots represent two shrinkage from baseline with longer downward bars reflecting a larger decrease in tumor size.

These data correspond to a confirmed overall response rate of 75%. The spider plot on the right shows tumor shrinkage over time. Again, we see most of the lines going down and tending to stay down over the period of evaluation. It provides an early glimpse of the durability of responses, even in patients having the harder to treat squamous cell histology.

And if we look at the panel on the bottom of the slide, these are data for the dose expansion cohort B, which started subsequent to cohort A and therefore has considerably shorter duration of fall at the time of the data cutoff. Nonetheless, even with very limited duration of follow-up, we continue to see encouraging early response rates in patients receiving '4404.

Next slide please. The observed safety profile shown here on slide 17, is generally consistent with the known safety profiles of chemotherapy combined with PDA-1 and angiogenesis inhibitors. The most common treatment-related adverse events are listed on the left hand side of the slide in order of decreasing frequency in patients receiving '4404. The aggregate frequencies are shown on the right. In purple for '4404 plus chemo groups and in gray for tislelizumab plus chemo groups. The hematologic adverse events were the most common type for both arms, consistent with the chemotherapy regimen.

In total, grade 3 and higher treatment related adverse events were observed in 39% of patients receiving '4404 at the 10-mg per kilogram dose level, versus approximately 33% in patients receiving the tisillizumab combination therapy. These grade 5 treatment-related adverse events occurred in patients receiving '4404 at the 10-mg per dose level, and in one patient receiving the tislelizumab combination. Importantly, treatment-related adverse events leading to drug discontinuation were low.

Overall, these phase two data are supportive of the promising efficacy and manageable safety profile for '4404 in combination with chemotherapy for patients with advanced non-small cell lung cancer, independent of tumor histology and independent of PDL1 expression. These results build upon the encouraging monotherapy for '4404 presented at ASCO earlier this year and strengthen our confidence in the selected dose for the planned Phase 3, pivotal trial.

Francesca DeMartino - *Pfizer Inc - Chief Investor Relations Officer, Senior Vice President*

And based on the data you just recapped, what's next for '4404 in lung cancer?

Jeff Legos - *Pfizer Inc - Chief Oncology Officer*

Supported by this very encouraging phase two data, we've worked with health authorities to design a single global Phase 3, study of '4404 plus chemotherapy in both squamous and non-squamous cell lung cancer. The design of this trial is shown here on slide 18. It will enroll patients with locally advanced or metastatic disease who have no known actionable genomic alterations and who have not received prior systemic therapy for advanced or metastatic disease.

Both PDL1 positive and PDL1 negative patients will be eligible. Patients will be divided into two cohorts based on histology and randomized to receive chemotherapy in combination with either '4404 or pembrolizumab. After the initial number of treatment cycles, patients will continue with maintenance therapy.

The study is designed to enroll about 700 participants in the squamous cell histology cohort and about 800 participants in the non-squamous cohort. The dual primary endpoints of the study are progression-free survival and overall survival. If successful, we believe this study could support potential approvals to first line studying for both squamous and non-squamous histology, non-small cell lung cancer.

As I previewed earlier, our plans with '4404 also extend to the extensive stage small cell lung cancer. If we flip now to slide 19, we'll see the design of our planned Phase 2/3 trial in this indication. This study will begin with a Phase 2 open label cohort evaluating '4404 in combination with chemotherapy.

If the data from the phase 2, part of the study are supportive, we'll then rapidly and seamlessly move into a phase 3 double-blind randomized portion. Here we will evaluate the combination of chemotherapy with either 4,404 at the Phase 3, dose or the anti-PDL1 monoclonal antibody otezallizumab. The primary endpoint of this trial will be overall survival.

If successful, we believe this study could support potential approval for '4404 in first line extensive stage small cell lung cancer and together with our non-small cell lung cancer study support our broader ambition to displace traditional checkpoint inhibitors in the lung cancer treatment paradigm.

Francesca DeMartino - *Pfizer Inc - Chief Investor Relations Officer, Senior Vice President*

Thanks, Jeff. To conclude, could you provide an overview of how your plans for '4404 fit within the broader lung cancer portfolio?

Jeff Legos - *Pfizer Inc - Chief Oncology Officer*

Absolutely, if we could just move to Slide 20, please.

So here we can see a summary of our approved medicines on our late stage lung cancer agents currently in development. Starting at the top, we have our approved targeted small molecule medicines. These include our Braftovi and Mektovi combination, which is approved to treat BRAF V600E, metastatic non-small cell lung cancer, and Lorbrena, which is approved for ALK positive metastatic non-small cell lung cancer.

Beyond our targeted small molecules, we're also developing '4404, as well as the antibody drug conjugates SV and PDL1V. Shown in the darker blue are the ongoing Phase 3, trials for SV and PDL1V in non-small cell lung cancer. The second line study of SV in non-squamous disease with any PDL1 status is anticipated to read out next year.

In addition, we've recently initiated both a frontline study of SV in patients with TPS eye disease and a histology agnostic second line and later study with PDL1V. There are also future opportunities for SV in the first line setting in patients with PDL1 low or PDL1 negative tumors.

We've just detailed our Phase 3, frontline studies for '4404 in both small cell and non-small cell lung cancer. However, we can also see the potential for '4404 in earlier settings of non-small cell lung cancer treatment. And of course there's the Phase 1, Phase 2 study that I mentioned earlier where we plan to begin exploring '4404 in multiple combinations, including those with our antibody drug conjugates where we have a growing body of data suggestive of potential synergy when combined with anti-PD1 therapy.

Francesca DeMartino - *Pfizer Inc - Chief Investor Relations Officer, Senior Vice President*

Thank you for that great recap of our lung cancer strategy, Jeff. Shifting gears, could we now speak about the colorectal cancer for which Pfizer is also pursuing a near term Phase 3, receptor '4404.

Jeff Legos - *Pfizer Inc - Chief Oncology Officer*

If we could advance to slide 22, please. Like lung cancer, colorectal cancer represents a significant unmet need and a substantial opportunity for new therapies. It's one of the most commonly diagnosed cancers globally, with more than 1.5 million new diagnoses expected in 2025 alone.

It's the second most frequent cause of cancer-related death in the United States, and despite recent advances, it continues to remain difficult to treat. This is particularly true in the metastatic setting, where the five-year survival in the United States is a dismal 16%.

Through our development of '4404, we hope to improve outcomes for patients with colorectal cancer and expand our leadership in a large and growing marketplace that has a projected 2030.

Francesca DeMartino - *Pfizer Inc - Chief Investor Relations Officer, Senior Vice President*

And the areas of the market where Pfizer is aiming to make an --

Jeff Legos - *Pfizer Inc - Chief Oncology Officer*

Slide 23. Here you can see that treatment of metastatic colorectal cancer, or metastatic CRC for short, is guided by various tumor characteristics and genetic markers. When considering unresectable or metastatic CRC, first line treatment typically involves systemic therapy with regimens that include chemotherapy, biologics, targeted therapies, and or immune checkpoint inhibitors.

Therapeutic regimens are driven by the molecular profile of the tumor being treated. One way in which metastatic CRCs are classified is by microsatellite instability or MSI high status. MSI high patients typically have deficient DNA mismatched repair systems and represents approximately 5% of metastatic CRC. These patients are often treated with immune checkpoint inhibitors, as MSI high status is a key biomarker to help predict response to these therapies.

The remaining 95% of patients are classified as microsatellite stable and are typically treated with anti-EGFR or anti-VEGF therapy. These patients will be the focus of our planned '4404, Phase 3, studies in metastatic CRC and as we will test dual anti-VEEF anti-PD1 regimen, including an anti-VEGF monoclonal antibody.

Metastatic CRC tumors are also classified by genetic mutations or amplifications. Focusing on where Pfizer medicines are having an impact. There are V600E mutations which affect about 8% to 10% of patients with metastatic CRC, and there are also HER2 positive metastatic CRC, which represents about 3% to 5% of CRC patients. With '4404, we aim to improve patient outcomes by building a diverse franchise that.

Francesca DeMartino - *Pfizer Inc - Chief Investor Relations Officer, Senior Vice President*

Okay, great. Thanks for that overview, Jeff. Can you next speak a bit about the data that supports your plans for '4404 and metastatic colorectal cancer?

Jeff Legos - *Pfizer Inc - Chief Oncology Officer*

Sure, if we if we turn to slide 24. Here we can see some of the data which were presented at the recent European Society of Medical Oncology meeting last month.

These data come from a Phase 2, trial in China conducted by 3SBio evaluating '4404 in combination with chemotherapy in patients with treatment naive metastatic CRC. Patients with an MSI high status were excluded from this study.

The results are shown from a cohort of patients receiving 10 mg per kilogram of '4404 every other week in combination with a modified FOLFOX chemotherapy regimen, which is the regimen we plan to take forward into Phase 3.

We observed encouraging anti-tumor activity in this study with a greater than 57% confirmed objective response rate and greater than 95% disease control rate achieved with our planned Phase 3, regimen. On the left, you can see the reflecting larger decreases in tumor size, and in the spider plot on the right, you can see the data capturing durability with many responses ongoing at the time of the data cutoff.

If we move to slide 25, here you can see data highlighting the manageable safety profile of '4404 plus chemotherapy in the Phase 2, study. In the interest of time, I'll highlight that with our planned Phase 3, regimen, we saw no grade 3 or higher immune-related adverse events and no treatment-related adverse events leading to '4404 discontinuation or death.

Looking across all dose regimens in the study, the proportion of patients with grade 3 or higher immune-related adverse events and treatment-related AEs leading to '4404 discontinuation or death, were very low at 2.3%, 1.1%, and 2.3% respectively. Together with the encouraging anti-cancer activity observed in this study, these results support our plans to evaluate '4404 plus modified Fol Fox in the Phase 3, trial.

Francesca DeMartino - *Pfizer Inc - Chief Investor Relations Officer, Senior Vice President*

Thanks Jeff. Could you please expand a bit on the design of the Planned Phase 3 study?

Jeff Legos - *Pfizer Inc - Chief Oncology Officer*

Of course, if we could just advance to slide 26, please. Here we can see an overview of our planned study in first line metastatic colorectal cancer. The study, which is currently posted on clinicalTrials.gov, is a global double-blind Phase 3, trial evaluating '4404 against the anti-VEGF monoclonal antibody bevacizumab, both in combination with modified FOLFOX.

Similar to the phase 2 study, this trial will exclude patients who are MSI-high, focusing on the population of patients where PD1, PDL1 checkpoint inhibitors have historically shown limited benefit. The study is designed to enroll about 800 participants and has dual primary endpoints of rent-free and overall survival. If successful, we believe this study could support a potential approval in first-line metastatic CRC, as well as our broader ambition to displace traditional anti-VEGF therapy in the metastatic CRC treatment paradigm.

Francesca DeMartino - *Pfizer Inc - Chief Investor Relations Officer, Senior Vice President*

Thanks, Jeff. This has been a very informative discussion. So to summarize our conversation today, I would say Pfizer Oncology is aggressively moving forward with an ambitious development plan to unlock value for our foundational asset '4404, aiming to generate data that could pending clinical and regulatory success, make it a backbone treatment across multiple cancer types.

At a high level, several parts of today's conversation stand out. First, '4404 is a seamless fit with Pfizer's oncology strategy, leveraging our deep expertise in both the development of multi-specific antibodies and in relevant disease areas, and the global development plan builds on a truly global R&D presence.

Second, a 3-pronged strategy is in place to execute the development plan. Speed is exemplified by 7 planned near-term clinical trial starts, including two Phase 3, studies in the first of many planned waves. Breath is demonstrated by the multiple tumor types in these planned near-term trial starts. And depth encompasses multiple treatment settings, lines of therapy, and the evaluation of novel combinations with our leading ADC portfolio within a given disease area.

Third, we continue to be rigorous in our approach to '4404's development, utilizing encouraging clinical results to make data-driven decisions and create an enabling framework for interactions with health authorities so that '4404 program may progress with both maximum rigor and speed.

And finally, the tumor types encompassed by the '4404 development plan are not only grounded in Pfizer's current commercial presence but also represent attractive opportunities in disease areas with a large unmet medical need. This is highlighted by the initial pivotal programs in lung and colorectal cancers, which are large and growing markets that may reach approximately $70 billion and $9 billion dollars by 2030 respectively.

We'll now begin the Q&A session with Jeff, Johanna, and Arati, and as a reminder, our Pfizer Pflash series is designed as an educational deep dive into our pipeline programs. I'll therefore kindly ask participants to keep questions focused on '4404 and the data and development plans discussed today and avoid questions that would require us to provide forward-looking financial projections. While we're happy to clarify any information we shared during the presentation, we will not be offering estimates beyond what has already been communicated.

Thank you for your understanding. With that, we're ready to take the first question. Operator, if you could please assemble the queue, and Jeff, I'll turn it over to you to lead us through it.

Jeff Legos - *Pfizer Inc - Chief Oncology Officer*

Thanks, Francesca.

QUESTIONS AND ANSWERS

Operator

(Operator Instructions)

Geoff Meacham, Citibank.

Nishant Gandhi - *Citibank - Analyst*

Hey guys, this is Nishant on for Geoff. Thanks for the question and useful presentation. So, my question is on the class overall. The PD1 x VEGF class is kind of becoming crowded in lung cancer. So beyond hitting the primary endpoints, are there any specific features on the final, like a label like superior safety or efficacy in key subgroup, or even those inconvenience that you believe will be essential for achieving, like dominant market share?

Jeff Legos - *Pfizer Inc - Chief Oncology Officer*

Thanks, Nishant, and maybe I'll start and then turn it over to Johanna. So, as mentioned, right, the trials are designed for superior, superiority with what we believe to be very clinically meaningful improvement in both progression-free survival and or overall survival or overall survival alone based on the exact design of the trial.

I think with respect to how we intend to differentiate here, I think we showed a few examples of combinations with standard of care and then ultimately kind of the next wave of innovation, we'll move into novel combinations. So we believe Through both very rapid and clinically meaningful improvements in our endpoints. We believe that will help us to differentiate as well as the novel combinations. But Johanna, I'll turn it over to you to share a little bit more with Nishant, how you're thinking about how else to enhance the label and success.

Johanna Bendell - *Pfizer Inc - Chief Development Officer Oncology*

Thank you so much, Jeff, and thank you so much for the question. I think first of all, when we think about how we ideally combine with our Pfizer portfolio and the next wave of innovation that Jeff was mentioning, we're really excited in particular about looking at combinations with our antibody drug conjugates. We're thinking about not only non-small cell lung cancer, but potentially other areas where Pfizer non ADCs are sitting in terms of the standard of care.

I think also in terms of subgroups that we would be thinking about for certain our trials will be planned for subgroups that we are considering to be able to preplan these and bake them into the clinical trial design so as you see the clinical trials coming forward, and if you want to understand a bit better the subgroups that we're looking at, you'll see those within not only the Phase 3, but also within the exploratory trials that we're doing so you can see different populations that we're looking for. We're always excited to try to think about bringing treatment earlier in the in the cancer setting to have even more efficacy for our patients.

When we think about safety, we've seen a differential where two antibodies, if we give a PD1 inhibitor and a VEGF inhibitor separately, we may have issues in terms of being able to maximize the efficacy for patients based on safety differentials that we see by giving two separate antibodies.

And one thing that we're very excited about with the combination of the bispecific is that we're happy, we're excited to localize the treatment effect more to the tumors to potentially decrease the safety issues that we could potentially see by treating with both a PD1 and a VEGF antibody alone. And then we're also very interested in tying into our trials the patient related outcomes to make sure that we're really seeing benefits for our patients, not only in terms of overall efficacy that we see within the clinical trials, but also in how they're feeling.

Operator

Steve Scala, TD Cowan.

Steve Scala - *Cowen and Company LLC - Analyst*

Thank you. I have a few questions. Do you think Phase 3, results in lung cancer will set the upper bound for efficacy for PD1 x VEGF, the whole class across tumors? And what overall survival hazard ratio do you need to see in lung cancer to be convinced that this class has transformative potential across tumors?

So, that's the first question. Second question is it possible that big centers will have competitive PD1 x VEGF trials, Ongoing. Some theorize the reason Keytruda had such a successful clinical trial program is that they got the best patients at each center. If you believe that is true, then how can Pfizer enjoy that same advantage?

Thank you.

Jeff Legos - *Pfizer Inc - Chief Oncology Officer*

Thanks for the question, Steve, and I try to capture them and if we miss any, just remind me. So, I think your first question with respect to will the Phase 3, results in lung cancer set the overall benchmark. So across multiple cancers. So I think we recognize that lung cancer has been one of the more immunogenic cancers where patients have responded to anti-PD1, so we believe this is an important first place to study the medicine, and it's the area where we have the largest proportion of Phase 2, data, but we also recognize that every cancer is different and every combination is different, which is why we have a very broad and deep development plan, because we don't expect to just extrapolate the results from one cancer to another.

And as you're well aware, colorectal cancer and non-small cell lung cancer are very different with respect to how patients respond to anti-PD1 or PDL1 therapies. In terms of the clinically meaningful benchmarks, I would just reiterate the point that I made previously in that here we are designing our studies based on the sample sizes that were shown to exhibit both a clinically meaningful and statistically significant benefit for patients with respect to our time to event end point.

I think your last question was around sort of clinical trial sites and potentially getting the best patients. I think the best patients aren't necessarily representative of real world patients, but that being said, I think this is where the breadth and the depth of our expertise across a wide range of cancers, including non-small cell lung cancer and colorectal cancer, will already help us in terms of having this established clinical trial footprint and deep relationships with these investigators.

And we have already identified more than 500 clinical centers who we have worked with across all of our previous studies who have confirmed their willingness to participate in these upcoming Phase 3, clinical trials. So we believe that we will be able to sort of reach and target patients that are truly representative of those which we are seeing an indication in, including both the United States, Europe, and Asia.

Operator

Evan Seigerman, BMO Capital Markets.

Evan Seigerman - *BMO Capital Markets - Analyst*

Hi guys, thank you so much for taking the question, and I will not ask a Metsera question. That's a joke, by the way.

You got it, it's been a week. It's been a week. But as I think about kind of the competitive landscape, kind of that, following off of Steve's question, we saw some data for the competitive Summit assets, at ESMO. Maybe put into context that data and how you think, your asset will. Be able to compete and really show that this is the PDL1 x VEGF bispecific and secondarily when you were evaluating potential assets to in-license, what were some of the unique features of this antibody that you know drove you to ink the deal?

Thank you so much.

Jeff Legos - *Pfizer Inc - Chief Oncology Officer*

Thanks for the question, Evan, and maybe I'll ask Arati Rao, who's our '4404 franchise lead, for this molecule to come in a bit on maybe some of the pre-clinical data and then what specifically excited her during diligence and then currently with respect to the clinical portfolio, where now I think more than 650 patients have already been treated with '4404.

So Arati, over to you.

Arati Rao - *Pfizer Inc - Thoracic Oncology TA Development Head'4404*

Thank you, Jeff. Thanks, Evan for the question. So in terms of the pre-clinical data, I will tell you that the unique tetravalent structure or a tetrabody that 707, '4404 is what attracted me when I first began looking at this package. This tetravalent structure allows for each arm to simultaneously bind PD1 and VEGF together. In the presence of VEGF 707 forms multims and this Multimoization or daisy chaining, as we call it, is what allows for increased affinity for PD1, and then that leads to increased binding of PD1 by almost 10x.

The, fully functional VEGF arm on this molecule is really interesting, and it actually, not only does it drive angiogenesis, antiangiogenesis, it also, creates an immuno inhibits this immunosuppressive environment that we see, in the TME. All of these, Pre-clinical, the preclinical data has really kind of attracted us towards it. The VEGF inhibition was a little more differentiated from some of the other molecules that we had seen.

That's all I could say. Your second, the second piece of this question that you had was how are we differentiating from some of the data that we saw at ESMO this year. And I'm guessing you're referring to the Harmony 6 study in squamous, non small cell lung cancer where Ivonescimab was combined with chemotherapy, combined, versus Pembro plus chemotherapy.

And what, tell you is that in our 98, we had 125 patients treated, with squamous non small cell lung cancer. 98 of those patients, were treated at the 10 mg per kg Q3 week FDA aligned dose now. And when we compare our small data set with the 260 some patients in the Harmony 6 arm, you can see that the overall response rate, and the, is similar in terms of the, is very similar.

Our follow-up is, needs to be longer, Because we are a little, of, slower, I mean, therefore ahead in development, but when it comes to the toxicities, it seems like the VEGF related toxicities, the all grades hemorrhage, hemoptysis, etc. Are very similar between the two, so as we kind of expand into, larger data sets, we expect that these will, bear out, and we'll see, really good efficacy and, toxicity, with our module.

Operator

David Risinger, Leerink Partners.

Jason Zhuang - *Leerink Partners LLC - Analyst*

Thank you. This is Jason Zhuang for Dave. I have two questions, please. So first of all, following up on the differentiation of, '4404 could you please provide a roadmap for potential validation of the superior efficacy and specifically key readouts to watch in coming years that, establish the

differentiation versus other specifics. And second, given private licensing agreement with 3SBio, please remind us about the economics for Pfizer and 3SBio. And Pfizer will book financials on the income statement.

Thank you.

Jeff Legos - *Pfizer Inc - Chief Oncology Officer*

No, thanks for the question, Jason, and maybe I'll start by addressing the first one and then maybe ask Francesca to come back in on the economics for the 3SBio deal. So first you talked about the roadmap here and I just want to remind the audience that this deal didn't close until sort of late July, early August this year and I am incredibly pleased and proud of which the speed that we were able to execute on a lot of the activities that we shared with you just over the past 3-months.

And if we think about what has been accomplished by then, we were able to sort of transfer all of the data, from our colleagues at 3SBio, prepare these 7 regulatory documents, file the 5 IMDs, and now are well equipped to have these 7-year term studies start, not to mention the tech transfer and the ability to sort of complete.

The first drug product manufacturing here in the United States. So, the first part of the roadmap is obviously the 7-year term study starts that we have highlighted today. In terms of data readouts, we will continue to follow the additional patients for both depth and durability from the ongoing Phase 2.

The next part of our roadmap I mentioned during the presentation is up to 10 additional trials. Starting in 2026 and up to 10 additional novel combinations starting in 2026. So continuing to build upon the momentum that we've all started just over the the previous three 3-months.

If we think about the kind of the overall trial readouts, most of these studies are Phase 3, studies with time to endpoints of progression-free survival, and overall survival, so I would just refer you to clinicaltrials.gov and look at the primary completion date as to when you could expect this data to become available. And maybe to your second question on the overall 3SBio economics and our deal terms.

Maybe I could invite Francesca.

Francesca DeMartino - *Pfizer Inc - Chief Investor Relations Officer, Senior Vice President*

To speak about that. Yeah, I can take it, Jeff. Okay, so thanks for the question. So this is a pretty traditional structure, so they're eligible to receive milestone payments associated with certain development, regulatory and commercial milestones.

I think those were all disclosed up front, and yeah, so that's pretty much the structure. So there's also tiered double-digit royalties on sales of '707, which we're now calling '4404. So if you want to reference, I think we disclosed those all in the initial press release, but pretty traditional structure.

Jeff Legos - *Pfizer Inc - Chief Oncology Officer*

Next question.

Francesca DeMartino - *Pfizer Inc - Chief Investor Relations Officer, Senior Vice President*

Please. Okay, I think we're actually, Jeff, I can close it because I think we're, that was our, -- no there's one more. I apologize. We just saw in the queue.

Operator

Chris Schott, JP Morgan.

Ethan Brown - *JP Morgan Chase & Co - Analyst*

Hi, this is Ethan on for Chris Schott. Thanks for taking our questions. Just maybe broadly, can you talk about how you think about the relative opportunities with '4404 either alone or in income with chemo versus kind of the opportunities you have in combination with your ADCs, and kind of in the context of increased competition with just the VEGF Bi --

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Jeff Legos - *Pfizer Inc - Chief Oncology Officer*

Yeah, thanks for the question, Ethan, and I'm happy to start just with a broad overview and then I'll pass it over to Johanna. So, as mentioned earlier, for both non-small cell lung cancer and colorectal cancer, despite the progress with chemotherapy plus or minus, immunotherapy and lung cancer are plus or minus bevacizumab and colorectal cancer.

Both of these represent a significant unmet medical need, and both of these represent a pretty rapid path to the initial approvals and development because they are simple add-on trial designs, so you're combining on top of the standard of care to hopefully improve, displace, or replace the existing chemotherapy regimens, and or in combination with with '4404.

As we think about the novel combinations, this is where the breadth and the depth of our portfolio represent a significant and unique opportunity for us to differentiate. So maybe Johanna, I'll turn it over to you to share a little bit more as to how you're thinking about the next wave of opportunities.

Johanna Bendell - *Pfizer Inc - Chief Development Officer Oncology*

Thanks so much, Jeff, and thanks so much for the question. I think one thing we're particularly proud of at Pfizer in terms of our antibody drug conjugates is data that we've seen combining the vedotin antibody drug conjugates with immune checkpoint inhibitors. We've already seen proof of this in the combination with our molecule bevacizumab and pembrolizumab, where we see improvement in the immunogenic potential of a PD1 inhibitor, particularly when combined with a vedotin payload.

Rather than a Topo1 payload, so we're hoping to not only take advantage of that vedotin ADC, but also with our novel targets for the vedotin ADC, such as integrated integrane beta 1 -- beta 6 with our SV molecule and PDL1 with our PDL1V molecule.

We also see across the spectrum of different tumor types areas where both antiangiogenic approaches and immunotherapy approaches work, and we're very excited for this molecule because we think that we have the potential to improve hitting both of these pathways.

And so as we start to think about the broad potential of these molecules being able to hit both of these pathways harder and potentially with less toxicity, we can think about a lot of different tumor types that could potentially benefit from this, not only in combination with our vedotin ADCs, but also in combination with other treatments such as the standard of care that Jeff was alluding to, as well as potentially with single agent.

Francesca DeMartino - *Pfizer Inc - Chief Investor Relations Officer, Senior Vice President*

Okay, great. Jeff, that was our last question. So I will, I just want to thank, Jeff, Johanna, and Arati again for joining us this morning. This was a really comprehensive overview and, for those of you that have dialed in and are sell-side analysts, thank you so much for your time and your engagement, and I hope everybody has a wonderful week and we will see you and talk to you soon.

Everyone can disconnect. Thank you so much.

Operator

This does conclude today's program. Thank you for your participation. You may disconnect at any time.