INFLO-1 Data Readout: Strengthening the Nintedanib DPI Opportunity in IPF

Mannkind | Jul 29, 2026

Operator (00:01):

Good afternoon and welcome to the MannKind Corporation conference call to discuss the phase 1b results for nintedanib DPI.

(00:08):

As a reminder, this call is being recorded on July 29th, 2026, and will be available for replay on the MannKind Corporation website shortly after this call for approximately 90 days.

(00:18):

This call will contain forward-looking statements. Such forward-looking statements are subject to risks and uncertainties that may cause actual results to differ materially from these expectations. For further information on the company's risk factors, please see the form 10-Q for the period ended March 31st, 2026, this morning's press release, and the slides prepared for this presentation.

(00:40):

Joining us this morning are Michael Castagna, chief executive officer, and Dr. Wassim Fares, senior vice president in Therapeutic Area Head Respiratory. I'd now like to turn the conference over to Mr. Castagna.

Michael Castagna (00:53):

Thanks, Operator, and good afternoon everyone. Thank you for joining us for this focus update on nintedanib DPI. I'll begin with the IPF opportunity and why we believe this program can create meaningful shareholder value over the coming years. Then Dr. Fares will review the clinical data, including our phase 1b results, as well as a history of the program leading into our global phase 2 now underway. I'll return with a few closing thoughts before we open up the call for questions.

(01:23):

Let me start with the broader context. At the beginning of the year, we laid out three major catalysts. We have now delivered on all three through July. The Afrezza Pediatric indication is now approved, expanding the population we can serve and creating a growth opportunity. We're excited about the early days of launch and we'll provide more details on our next week's earnings call. Furoscix ReadyFlow is approved, reducing administration from hours to seconds while supporting broader adoption and operation in health systems, as well as a lower cost of goods.

(01:58):

Two approvals in a single year is allowed for a company of any size, let alone ours, which brings me to nintedanib DPI. When we called this update, we've completed the third catalyst on this page, and it's the one we spent the last seven years to get to this point. There's an urgent need for new effective therapies in IPF, and we believe lung-targeted delivery is the best approach that addresses the tolerability barriers that are holding today's therapies back. For us, our phase 1b data is the key clinical de-risking step for the entire program and it's the reason we want to walk you through the history and the full picture where we are today.

(02:37):

Let's begin with the opportunity. The first is that our phase 1b study demonstrated safety and tolerability in patients with IPF. That's a data set we haven't had. And I'm proud to say there were no serious adverse events, no GI issues, and no patient discontinued.

(02:55):

Dr. Fares will take you through the details shortly, but I'd summarize it this way. The tolerability questions we and our investors have cared about, including inhaled antifibrotic therapy in the lungs, are precisely the questions the study was built to address. And the results give us the confidence to advance this program forward. Our global phase 2 is underway and we are actively progressing site activations and we expect enrollment to continue to increase as we progress through 2026.

(03:25):

I want to spend a minute why we're investing here. It's because IPF is a category that has already been commercially validated. We don't have to establish a disease state. These are approved therapies in the market today, and OFEV has generated more than $4 billion in global revenue just in 2025. And I hear JASCAYD is off to a fast start approaching $2 billion in their first year of launch. You have a blockbuster precedent and a disease with roughly 100,000 IPF patients in the US, a population that unfortunately continues to rise year after year.

(03:59):

Beyond IPF itself, there's a larger adjacent segment of patients with pulmonary fibrosis, more broadly, interstitial lung diseases that can lead and progress to fibrosis. So the market does not need to be created. The disease burden is clear. The treatment categories established. The unmet need remains substantial and unchanged. And that combination creates an opportunity for a targeted inhaled delivery.

(04:23):

Let me be a little more specific about the challenge we face because it's not a problem of efficacy. Nintedanib works. We don't question that. It's the first drug to really show what it can do to help patients. The problem is patients can never start therapy because they know the side effect profile or they don't stay on therapy. Three out of four IPF patients are not on an approved antifibrotic therapy despite the fact that 80% face the risk of death within five years of diagnosis. Among those who do start, published discontinuation rates run as high as 50%, and current therapies carry major tolerability challenges.

(05:03):

Our aspiration was to take a proven molecule, change its route of administration to solve this unmet need created by the standard of care. Nintedanib DPI is designed to deliver drug directly to the deep lung where fibrosis occurs while bypassing the GI tract and reducing systemic exposure. The GI adverse effects associated with oral nintedanib are the reason so many patients stop or never want to start. So reducing systemic exposure is the mechanism by which we hope to change the treatment experience. We believe this approach has the potential to improve efficacy and tolerability, which may support long-term adherence. This thesis has recently been proven out by the data released on inhaled pirfenidone as well as TYVASO's TETON-1 and 2 trial, all of which show that targeted lung delivery therapy does drive efficacy in IPF. With these phase 1b results, we have more confidence in our program and why this target approach will have an impact on patient outcomes.

(06:04):

The reason we believe we can execute on this thesis is the platform underneath it. Technosphere technology provides highly efficient delivery of a dry powder through a small portable device that we

call Dreamboat. The FDK microparticles at the core of our technology drive rapid uniform distribution deep into the lung with extensive throughout the lung tissue. Often I get asked, "Can they inhale a dry powder? Will they receive the product?" And the answer is yes. If air is flowing, our powders are going into that area of the lung. It's already been validated on two FDA approved products, Afrezza and Tyvaso DPI. For us, that changes the CMC and drug device risk profile of a program like this considerably. We're not simultaneously trying to prove a new delivery technology and a new molecule and a therapeutic hypothesis. We know how to formulate this on our platform. We know how to manufacture at scale. We have real world data experience and how patients use our inhalers day in and day out.

(07:02):

For a chronic disease where patients may be on therapy for years, the practical characteristics of the device, the portability, the fast inhalation are not a footnote. They are part of whether a therapy gets used at all.

(07:16):

One technical point worth understanding is the versatility of the platform. A Technosphere particle and the products that we make are mostly FDKP-based carrier with a small percentage of active drug, as you can see here. Technosphere powder has now been used in more than 50,000 patients, a substantial base of experience with the carrier itself before we ever put nintedanib on it. This gives us ability to really understand where our particles go, how they are formed, and how patients can tolerate them across multiple diseases.

(07:49):

I also want to address a question we get regularly, which is, whether patients and prescribers will adopt a dry powder inhaler. We have a case study from our own experience in the inhaled treprostinil market where DPI today has grown to 80% of the market since launch. Patients have demanded this, patients have enjoyed it. In this pulmonary population, many of them elderly, many of them with compromised lung function, the DPI format has become the dominant way the therapy is delivered.

(08:18):

I'm not going to claim that history will repeat itself automatically in IPF, but it does tell us something important about behavior. When a dry powder option offers a genuinely better experience than the alternative, clinicians prescribe it and patients demand it. Those dynamics give us confidence in the commercial logic behind nintedanib DPI, assuming we deliver the clinical profile we're working towards.

(08:40):

With that said, let me turn it over to our clinical data. I'm pleased to introduce you to Dr. Wassim Fares, who joined us a little over three years ago to lead our respiratory therapeutic area. Dr. Fares is a board-certified pulmonologist with more than 18 years of running respiratory clinical development programs in PAH, IPF. From early stage studies all the way through phase 3 and post-approval, he has spent a career on serious rare lung diseases across both academic medicine and biopharma. So he understands the challenges patients face, how to develop drugs, and how to get these to patients in the quickest way possible.

(09:17):

Thank you, Dr. Wassim, for joining us today, and I will turn it over to you.

Wassim Fares (09:20):

Thank you, Mike. Good afternoon, everyone.

(09:23):

Before starting the clinical program in humans, we conducted multiple animal studies to characterize the pharmacokinetics, pharmacodynamics, and safety of an internal dry powder inhalation. In these preclinical studies, which included five non-GLP, GLP stands for good laboratory practice, and three GLP studies, lung concentrations were at least 100 fold higher than plasma with minimal systemic exposure. We did 28 day toxic studies in two different species and a six-month repeat dose study. These studies showed no clinical toxicity and they established a wide safety margin, which was the pharmacokinetic and safety foundation we needed to move into humans.

(10:14):

Since then, our clinical program has advanced from first in human healthy adult volunteers to patients living with IPF. We published the results of the Healthy Volunteer study along with the preclinical studies earlier this year. And we are reporting today the results of INFLO-1, the phase 1b study that showed safety and tolerability of nintedanib DPI in patients living with IPF.

(10:42):

We are now enrolling in INFLO-2, our global phase 2 study for patients with IPF. In less than two years, the program has moved from first in human dosing to a global phase 2 study, which we are very proud of. The team has done an exceptional job with this progress. In the next few slides, I will go into more detail into each of these studies in humans.

(11:11):

Starting with the first in human study, it used a standard stepwise design. Part A evaluated single ascending doses from 2 to 8 milligrams. After formal safety reviews, part B evaluated twice daily repeat dosing over seven days. The objectives were safety, tolerability, and pharmacokinetics, not efficacy. We wanted to know whether we can deliver enough exposure in the deep lungs where IPF pathology is, whether exposure increased predictively with dose, and whether repeated delivery into the airways produced any signal of concern. Nintedanib DPI was safe and well tolerated

Wassim Fares (12:00):

... tolerated over seven days in healthy adults with no safety signals, no serious adverse events, and no study drug discontinuations. We observed mild reversible cough typically after the first dose without worsening on repeat dosing. We did not observe the systemic adverse events commonly associated with oral nintedanib, including diarrhea, nausea, vomiting, or headache. This was a short study in healthy volunteers, so it cannot establish chronic tolerability, but it provided the first human evidence that the formulation behaved as intended and supported advancement into patients with IPF.

(12:48):

Before I remind you of our PK data that we published earlier this year, I want to highlight the importance of nintedanib Cmax, which supports a lung-targeted approach. Published preclinical work shows that peak lung concentration, that is Cmax, is more important to nintedanib's antifibrotic activity than total exposure over time. That is AUC. In those models, brief high concentrations were sufficient to inhibit fibrotic pathways, while additional ongoing exposure beyond the peak did not add much. That creates a rationale fit for inhaled delivery. Achieve a high brief concentration in the lungs while limiting prolonged systemic exposure.

(13:39):

Our human pharmacokinetic data are consistent with efficient drug lung delivery. For inhaled nintedanib to reach the blood, it must go through the deep lungs first, including alveoli, pass through the lung

interstitium where IPF pathology is, and then cross to the blood. So plasma levels are an excellent surrogate of how much a drug is delivered to the deep lungs.

(14:05):

To orient you to this figure, our PK data are on the left. The ones on the right are published data from a nebulized nintedanib formulation. At comparable doses, nintedanib DPI produced plasma Cmax values approximately six to eight times higher than published values for nebulized nintedanib. This is a cross-study comparison, not a head-to-head trial, and it should be interpreted accordingly. What it shows is that the Technosphere formulation is delivering drug efficiently to the deep lungs with an immediate plasma peak.

(14:50):

Now, let's turn to the study most relevant to today's update. INFLO-1 was a randomized double-blind, placebo-controlled Phase 1B study in 27 patients living with IPF across 10 sites in the United States. Patients received one of two active regimens or placebo over seven days with formal safety review by the sponsor, us, and an external data safety monitoring board before dose escalation. The study was designed to assess short-term safety, tolerability, and pharmacokinetics. The gating question was simple. Can a fibrotic lung tolerate repeated administration of nintedanib DPI? The answer from this study was a clear yes.

(15:44):

The safety profile was clean. There was no drug-related diarrhea, nausea, or vomiting. As you know, these are the major adverse events that limit the use of oral nintedanib. There were no bronchospasms, no changes in oxygen levels or respiratory rate, and no study drug discontinuations or dose reductions. This is a meaningful de-risking step as we move into Phase 2

(16:17):

Let me address cough directly because it is the most common question about delivering a powder into fibrotic lungs. Approximately 60% of patients living with IPF who received active drug in this study had no cough. Roughly 90% had either no cough or only a mild, that is Grade 1 cough adverse event. None had a severe cough. When cough occurred, whether in this study or in our other studies using Technosphere technology, it generally followed the first dose and did not worsen with continued dosing. There were no discontinuations, no dose reductions, and there was no correlation between cough and powder mass. The observed pattern is consistent with prior experience across our Technosphere platform where clinical data from approved products show less than 3% discontinuation due to cough.

(17:23):

The extent of patient exposure also matters. Let me orient you to this figure. Magenta color reflects exposure in our trials with nintedanib DPI. Gray color reflects reported exposure by a nebulized nintedanib formulation. On the left, it shows exposure in healthy volunteers. On the right, it shows exposure in patients living with IPF. Across INFLO-1, we administered around 448 inhalations of nintedanib DPI to patients with IPF. I'm not talking about exposure in healthy volunteers. I'm talking about patients with the target disease, idiopathic pulmonary fibrosis.

(18:11):

Contrast this with what has been reported with a nebulized nintedanib formulation. We could find that only six doses were given to patients living with IPF. One dose per patient for six patients with IPF. As you know, exposure and clinical experience in patients with the target disease are very important. With that exposure to nintedanib DPI, we saw no difference in spirometry between active drug and placebo, which use an empty cartridge.

(18:45):

For clinicians evaluating an inhaled therapy in a compromised lung, that is an important pulmonary safety observation. This provides an impressive early safety database in the target population using a carrier already experienced by thousands of patients living with ILD through Tyvaso DPI in PH-ILD.

(19:11):

With that strong foundation, let me turn to Phase 2. INFLO-2 is a randomized double-blind, placebo-controlled global study that will enroll 210 patients with IPF. The 12-week controlled period evaluates two active regimens against matched placebo, followed by a 24-week open label extension. So at the end of that trial, we will have safety and efficacy data in patients with IPF over a nine months period. The primary objective is safety and tolerability with forced vital capacity or FVC as the key efficacy endpoint. Importantly, the study includes patients who are untreated, that is they are not on background IPF therapies, as well as patients who are on stable background therapy of Pirfenidone and/or JASCAYD. That design reflects the evolving IPF treatment landscape and preserves our ability to understand nintedanib DPI, both as an alternative first line antifibrotic and as a potential backbone for combination therapy. With that, I'll turn the call back to Mike.

Michael Castagna (20:31):

Thanks, Wassim. Let me close how we think about the value here. First, on patent protection, we've built a layered patent estate specific to nintedanib DPI in combination use with the longest dated protection extending to 2046. Underneath the product estate sits the platform itself with more than 1,400 patents enforced worldwide. And I'd like to add one point beyond patents. Manufacturing this powder at scale is genuinely complex, and that complexity adds a practical barrier to entry. We spent 35 years building the capability to make it at scale, and it isn't something a competitor can quickly stand up.

(21:13):

Nintedanib DPI is designed to be delivered in seconds and give patients lung-targeted delivery without the nebulizer burden or the systemic adverse events associated with oral therapy. Our Technosphere particles are already validated in two FDA- approved products used in the adult population, including elderly individuals with compromised lung function. And this overlap is within our target population is really relevant to where we're going. We also have experience in this clinical setting and our platform has demonstrated safety and tolerability in patients with underlying lung diseases. Tyvaso DPI is approved in PH and PH-ILD, which includes patients who also live with IPF in some cases.

(21:59):

Nintedanib is the gold standard in this disease, but the GI burden of the oral caps how much it can be used. I've never believed the sealant of this molecule was scientific. It's always been tolerability, and that's been going on for over a decade. At the same time, IPF is moving towards combination treatment as more options become available. We've seen the same progression across other chronic conditions, including respiratory disease, where monotherapy comes out and establishes a category, new mechanisms enter, and combination therapies follow. This is further evidenced as we look at the data just recently presented in TETON-1 and 2 that showed using combination use and IPF got additional effect size for patients.

(22:45):

Our thesis is that a well-tolerated, seconds-long inhalation nintedanib can become the backbone of future regimens. If patients are going to receive multiple therapies, the foundation needs to be effective, practical, and something they can remain on. That is our strategic thesis, not a demonstrated

outcome, but explains why we've designed our Phase 2 the way Dr. Fares described it, preserving the ability for combination approaches as well as monotherapy.

(23:14):

Finally, I want to zoom out because nintedanib DPI isn't our only exposure to this market. We have three shots on goal when we look at the IPF landscape, all of them running on our proven platform aimed at large underserved market. Nintedanib DPI is the asset we fully own. Tyvaso DPI through our partner with United Therapeutics is approved today with potential future expansion in IPF. And we recently announced in partnership with United Therapeutics, the Ralinepag DPI that is progressing towards IND.

(23:45):

Each of these programs draws in the same formulation science, the same manufacturing base, and the same clinical experience delivering dry powder into compromised lungs. The scientific and operational learnings from any one of these carries into the others.

Michael Castagna (24:00):

We're applying a large single capability across the same market, multiple angles from our lead asset as well as our partner programs. None of this guarantees clinical or commercial success, but it means we have a shot to make this very successful to help patients. With that said, operator, I'm going to turn it over and open it up for Q&A.

Operator (24:24):

Thank you. At this time, if you would like to ask a question, please click on the raise hand button, which can be found on the black bar at the bottom of your screen. When it is your turn, you will receive a message on your screen from the host allowing you to talk and then you will hear your name called. Please accept, unmute your audio and ask your question. We will wait one moment to allow the queue to form. Our first question comes from Ben Burnett with Wells Fargo. Please unmute your line and ask your question.

Tien Chi (25:12):

Hi. Hello. Can you guys hear me?

Michael Castagna (25:14):

Yeah. Yeah, we can hear you.

Tien Chi (25:17):

Hi. This is Tien Chi calling in for Ben. Congrats on the data team. So, I really appreciate the color that you provided on PK comparison versus the nebulized nintedanib. So, just curious, have you guys conducted an analysis or comparison versus the oral one? How does it look like?

Michael Castagna (25:39):

I think I have to go back to our animal talks. Our animal program is probably where we would compare to oral, but in humans, we've not done that because we're not trying to match plasma PK per se. And the data on plasma is out there publicly on oral, so there was no need to redo that work.

Tien Chi (25:57):

Got it. Got it. Thank you. Another follow up is, so now that you have this new data set. How did that change your thinking around expectation for the phase two data, whether it's safety or efficacy? Any updated thoughts over there?

Michael Castagna (26:18):

I don't think it changes how we're. I mean, we started the phase two in parallel at risk knowing that this result will come out somewhere in the middle or before we started the trial. It doesn't fundamentally change anything. If anything, it gets us more excited to go faster. And that's really what we're evaluating is now that we have 100% confidence on lung... The number one question we get is cough tolerability. Can patients who IPF do this? I think we can clearly say this after over, what, about 50 patients and hundreds of doses. We feel very comfortable going forward and we're trying to see how we can accelerate this as quickly as possible.

Tien Chi (26:54):

All right. Thanks for the color. Congrats again on the data.

Michael Castagna (26:57):

Thank you.

Operator (27:13):

Our next question comes from Olivia Brayer with Canter. Please unmute your line and ask your question.

Olivia Brayer (27:19):

Hey, good afternoon. Thank you, guys, for the questions. I want to drill down a little bit more on the adverse event data. I don't know how much more granular you can get or if you're planning to provide an events table at some point, but maybe just on the cough, can you characterize whether that 10% cough rate, was it all deemed treatment-related? And then for those 60% with no cough, is that just no cough whatsoever or just no worsening cough from baseline? And then I also wanted to ask, it sounds like you saw a cough almost immediately after the first inhalation in those patients that did have it, but was any of it transient or did it resolve over time?

(28:02):

Just trying to understand the comments made around it mostly not worsening. And then I've got a couple follow-ups, if you don't mind.

Michael Castagna (28:10):

Great, Olivia. I'll get some comment and then I'm going to turn over to Wasim to give further dialogue. The first I want to say is that the cartridges are 10 to 20 milligrams in powder per episode. So, we're talking about every time you gave an administration, you might have got one cartridge and two cartridges. And so, think about the powder load and the incidence of the number of cartridges. I'll let Wasim talk about the data behind the cough as he's closer to it. So, Wasim?

Wasim (28:34):

Hi, Olivia. Good to hear from you. As you mentioned, 60% did not have cough reported as an adverse event. So, what that means, if they had cough as a baseline, it did not get worse. It was cough related to IPF. Or if they did not have cough, it did not cause cough. So, that's one of the question. I think the first

question was we would report more details about this study in upcoming scientific conference. And then the others, the remaining 40% who had reported cough were deemed related to the study drug. Yes. The three quarters of those were mild. Most of them were also transient.

(29:17):

So, it was like an irritation after the first inhalation for most of these patients. Did I miss any of the questions, Olivia?

Michael Castagna (29:32):

Olivia, did we get all your questions? You might be on mute.

Olivia Brayer (29:38):

Oh, sorry. Can you guys hear me?

Michael Castagna (29:40):

Yeah, now we can.

Olivia Brayer (29:41):

Hello?

Michael Castagna (29:42):

Yep.

Olivia Brayer (29:43):

Okay, perfect. Yeah. Just to clarify on that. So, that final 10%, that is for the cough, right? Is how you guys are characterizing that? 30% mild, 10% moderate?

Wasim (29:58):

Yes. Yeah. 30% had grade one mild, 10% were moderate.

Michael Castagna (30:04):

And really, this is very subjective on cough, right? So, if you want versus a continued cough could make a difference. But they were all mostly transient. I think that's what's most important. These are not adding a huge burden to the patient. They're mostly reaction after inhalation.

Olivia Brayer (30:22):

Okay. And then wanted to ask on your PK data, if you're achieving six to eight times higher plasma exposure than nebulized nintedanib, how are you thinking about the balance between maximizing lung exposure and then obviously minimizing systemic exposure, just given that I know one of the major goals of the inhalation approach is to avoid some of those dose-limiting toxicities that we've seen with the oral therapy?

Michael Castagna (30:51):

Yeah. I think a couple questions came in on the adverse event table today. And I would say there's not much there to get excited about to want to share that. So, there's really nothing there. So, it's not like we're hiding something that we saw that you didn't hear about. Sorry. The question was what-

Wasim (31:13):

What PK.

Michael Castagna (31:14):

Oh, the PK, sorry. What I was going to say is it's 5% bioavailable from the oral. So, when you think about what we were trying to do is take that 5% bioavailable and put it directly into the lung. We have a long way to go to worry about hitting near plasma concentrations of what an oral nintedanib will get through the absorbed GI tract. And so, we've done the tox studies. We found we can go pretty high on dosing. There's a pretty high level of safety margin here that we're well below. And we're nowhere near a critical threshold of causing side effects in the systemic system or even lung issues, I'd say. So, we feel pretty good that those levels are. We're happy to see them, number one.

(31:54):

And it just is reinforcing our technology, which we really believe adds consistency in delivery. And that's something we could develop nebulizers if we though they were better and we did in the case of clofazimine, if you recall. But we always know that our technology delivers consistent deep lung penetration, where you're getting most of the powder into the lung and you're not losing it in the oral cavity, in the throat and the GI tract. You're getting most of it into the lung tissue. And that's really what our technology is about.

(32:21):

And that's really what I thought you could see here when you can see we're getting to the deep [inaudible 00:32:25], we're getting picked up in the blood, and we're showing the demonstration of that technology. And as Wasim said, getting through that lung interstitial layers shows up in the plasma. And that's what you should be confident in with our technology.

Olivia Brayer (32:41):

Okay. Thank you guys. Appreciate it. And congrats on the update.

Michael Castagna (32:44):

Thank you.

Operator (32:47):

Our next question comes from Roanna Ruiz with Leerink. Please go ahead and unmute your line and ask your question.

Ryan (32:57):

Hey guys, you have Ryan on for Roanna, and thanks for taking our questioning. Congrats on the update. Maybe just two from our end. How do you guys expect this seven-day safety cough data to translate into a longer 26-week and eventually a 52-week trial? Do you think the seven days provides a good benchmark for what we would see on this AE profile moving forward? And then a second one's just curious on the phase two. So, about your expectations for the two different dose arms, I believe it's four mgs twice a day and two mgs four times a day. Are you expecting differences in safety and efficacy

between those two, given the total dose is relatively similar? Or just curious your expectations there. Thanks.

Michael Castagna (33:42):

Yeah. The first thing I'd say, Ryan, is we're very thankful. We have thousands of patients from all the trials we've done over the 30 years showing that the cough is usually transient. It's immediate after the inhalation and it usually gets dramatically reduced after the first week. So, for us, the first seven days are actually the most important when we think about a long-term program because even you took Afrezza where we spent $75 million doing a multi-thousand patient trial. The first seven days, you see one out of four patients have a cough and it drops to less than 3%, 5% at the end of 30 days.

(34:16):

So, the cough here doesn't get worse with time. The powder loads aren't going up with time. Patients could have down-dosed in this trial if they were having trouble with cough or tolerability. Not one person did in either phase trial. So, I do believe the first seven days are enough for us to project out in the trial. And we didn't see any major concerns or major patient tolerability issues that give us concern. So, I do think that's predictive. I don't know, Wasim, if you have any-

Wasim (34:41):

Yeah, I agree. It's consistent with our prior data where the cough starts early on and it doesn't really get worse over continued exposure.

Michael Castagna (34:49):

Yeah. Thank you. And that was true in the patients who even did have cough, right? We didn't see it get worse. If anything, the first dose was their challenge and got better each one. And then the expectations you're asking, which I think is a great question on, do we expect a difference in the four milligrams twice a day or two milligrams four times a day? The answer is given the levels we're getting with each of our doses, no. But if C max really does have a certain critical threshold, maybe we'll see a slight difference in the four milligram where you might get a higher C max.

(35:20):

But what we're really testing here, because theory in animal models and cellular models don't always translate to humans, is we really don't know on the tetanum. Nobody does, but we do want to make sure we're covering the frequency of receptor engagement, the C max of receptor engagement, as well as matching up what's out there in the standards of care. We fully expect Tyvaso to do an incredible job in IPF. And we want to make sure that that's going to be out there used four times a day, that our product could potentially be used right next to it four times a day. And so, that's really the key of that second arm there.

(35:52):

QID is making it easy for the patient to remember when to take their drugs. My background's on HIV where people were taking 20, 30 pills a day,

Michael Castagna (36:00):

... Three different drugs. It's very hard for patients. And so how do we design things early so that when the data reads out, it's meeting the standards of care that are out there at that time? And we think that's critical. So we hope both work. We may find out one works better than the other or they're both comparable, but I don't expect from what we saw any differences in cough or tolerability so far. Our

seven-day data would indicate we should be confident in tolerability of either dose, but we'll be curious about efficacy as much as anything.

Ryan (36:31):

Awesome. Congrats again.

Michael Castagna (36:33):

Thank you, Ryan.

Operator (36:36):

Our next question comes from Brandon Folkes with H.C. Wainwright. Please unmute your line and ask your question.

Brandon Folkes (36:47):

Hi, thanks for taking my question. Maybe just a follow-up on the cough question. Granted, it is a small patient population, but in the patients where you did see mild to moderate cough, was there any potential trend or emerging trend in disease severity or any other patient baseline characteristic? Thank you.

Michael Castagna (37:06):

I'm going to turn that one to Wassim.

Wasim (37:09):

Thanks, Brandon. I mean, again, the sample size is small as you know, but within that sample size, there were no specific characteristics or trend that would differentiate or predict who's going to have a cough or not.

Michael Castagna (37:29):

Thank you, Brendan. Next question.

Operator (37:33):

Our next question comes from Yun Zhong with Wedbush. Please unmute your line and ask your question.

Yun Zhong (37:39):

Hi, good afternoon. Thank you very much for taking the questions and congratulations on the data. The first question is I wanted to confirm, did you see any FEV1 decline in any of the treated patient in the study? And the second question is, looks like while the study did not enroll patient who have had exposure to oral nintedanib, and looks like the ongoing phase 2 study is also having the same criteria. So I assume probably don't have any impact on the potential label in the future, but just curious, is that the same approach that the nebulized program is also taking in terms of patient enrollment? And what kind of impact do you think that criteria will potentially have on the pace of patient enrollment? Thank you very much.

Michael Castagna (38:27):

Yeah. I'll try to take these one at a time. So in the FEV1, this data will all be shared at a future scientific conference. I think Wassim presented somewhere in one of the slides that the difference between placebo, which was an empty cartridge and our active pattern was no difference in pulmonary characteristics. So we'll share more of those details at a conference, but that's all I can say for now. The next one was around exposure to oral. I can't remember. They couldn't be on the nintedanib, but they could have had it in the past.

Wasim (39:00):

They could have had it previously, but currently they're not on it or they were never on oral nintedanib in our trial.

Michael Castagna (39:06):

Yeah. But some patients could have tried oral nintedanib in the past. They just couldn't be actively on it because we didn't want to add to the burden of any potential side effects and really look at a clean profile here. So that is true in our standard trial. It's actually one of the major reasons we went X-US is because we wanted to be able to be used on the background of standard of care and/or naive patients. And we think a placebo controlled trial really can't go for 52 weeks in the US or even 26. So we got to the lowest we could, which is 12. And that's acceptable so far outside the US and we're working with the FDA to get that acceptable here. And so they could have previous exposure to nintedanib. They just can't be on active nintedanib. But within our trial, they could be potentially on [inaudible 00:39:49] or Jascayd and some of the newer agents will be moving that in any protocol changes going forward.

(39:54):

Those will be options. So we plan to have roughly 75% on some kind of background therapy at some point and probably 25% truly naive. That is different than the competing program out there. I believe they're going after only naive patients not on background therapy. So those are two different characteristics. I don't think one's right and one's wrong, but we'll see if they impact either company's enrollment. But I think this is a tough population to find for trials and we're going to do our best to get this done as quickly as possible.

Yun Zhong (40:28):

Great. Thank you.

Michael Castagna (40:30):

Thank you.

Operator (40:31):

Our last question comes from Gregory Renza with Truist Security. Please unmute your line and ask your question.

Gregory Renza (40:39):

Hi guys. It's [inaudible 00:40:40] for Greg. Congrats on the data today and for taking our question. Mike, at the top of the call, you mentioned you guys have been following 201 and studying this asset and opportunity for a while. So even though this is phase 1B data, I feel like this question is relevant. Do you see nintedanib DPI primarily as a switch play for Ofev intolerant patients as a first line alternative or an add-on that enables combination of other anti-fibrotics? And where do you see the initial commercial

point of entry just given the clean GI profile and compelling nature of the data to date? Thank you so much.

Michael Castagna (41:18):

Yeah. I think there's a lot that's going to change over the next three to five years while this program's going through development. If you ask me in general, I would say I believe nintedanib is the major background treatment in most clinical trials. I believe will continue to be the first choice for patients and doctors. Jascayd may make that a little bit different. We're seeing very fast uptake there. It's too early for me to see the data to say, is that coming 100% naive or switch patients? But I would say that that product is not as efficacious, but it's way more tolerable. And you're seeing that fast uptake on tolerability where people would rather take a more tolerable product and have something than nothing, right? And I think that's good for patients. But I see nintedanib being used as the background. I see DPI as becoming a predominant choice if the data pans out the way we expect, because patients really do not tolerate the oral.

(42:13):

And if they do tolerate it, it's through a lot of sacrifice. It's through a lot of the Imodium they take and other tricks in diet that they're doing everything they can to maintain that drug because they want to preserve as much life and lung function as possible. And so I think when they have an alternative to all that lifestyle, they will take it. Now, not every patient has that experience and not every patient struggles. And so those patients, if they're happy, they'll stay on what they're doing. And dry powders will be the first to say are not for every patient every time, but the large majority of patients can tolerate them and will tolerate them. And so we believe this will be a foundation opportunity. My guess is we'll get a good share of naive patients, we'll get a good share of intolerable, and we'll get a good share of patients who tried nintedanib and stopped for whatever reason.

(42:58):

So we see this as a large opportunity. Mostly will be used in combination by the time this gets to market as we see this being a combination market, which is why we are studying it in different dosing regimens. So we're excited and we're excited by the category and we're excited that the number of question we get is cough. And that was such an important topic to get out there today, as well as all the background data we've generated because people... We've not been always as fluent on this one and sharing with shareholders. We might have to take today to dedicate the background that we've done, the time we've been working on this and the insights we have. And hopefully that summary today is helpful for shareholders and ultimately investigators and patients.

Gregory Renza (43:41):

Thanks guys.

Operator (43:44):

That concludes the question and answer portion of today's call. I will now hand the call back to Michael Castagna for closing remarks.

Michael Castagna (43:51):

First, I'll say thank you to everyone for joining. We've had quite a few calls and data readouts and updates the last six weeks. And we have one more with an earnings call next week. And then we have September investor meetings kicking off. So a lot of great things happening here at MannKind. And we

just have never been more excited about the direction we're going, the number of patients we can help and where the shareholders should hopefully start to see the growth they've been waiting for. I want to thank the patients and investigators in Inflow One. And as we kick off Inflow two, this data doesn't exist without them. Our clinical data and manufacturing teams and clinical teams have been working really hard to make this program hit the timelines we set out for. And the first in human global phase 2 is off and running.

(44:32):

We're looking forward to updating you as enrollment progresses. And we'll talk to you all on the earnings call next week with additional questions. Feel free to email our IR inbox and we'll talk to you soon. Have a great afternoon and thank you again for joining today.