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PRESENTATION

Operator

Ladies and gentlemen, thank you for standing by. Welcome to the Royalty Pharma Fourth Quarter Earnings Conference Call. I would now like to turn the call over to George Grofik, Senior Vice President, Head of Investor Relations and Communications. Please go ahead, sir.

George Grofik *- Royalty Pharma plc - Senior VP and Head of IR & Communications*

Thank you, operator, and good morning and good afternoon to everyone on the call. Thank you for joining us to review Royalty Pharma's Fourth Quarter and Full Year 2021 results. You can find the press release with our earnings results and slides to this call on the Investors page of our website at royaltypharma.com.

Moving to Slide 3. I would like to remind you that information presented in this call contains forward-looking statements that involve known and unknown risks, uncertainties and other factors that may cause actual results to differ materially from these statements. I refer you to our 10-K on file with the SEC for a description of these risks. All forward-looking statements are based on information currently available in Royalty -- to Royalty Pharma, and we assume no obligation to update any such forward-looking statements.

Non-GAAP financial measures will be used to help you understand our financial performance. The GAAP to non-GAAP reconciliations are provided in the earnings press release available on our website.

With that, please advance to Slide 4. Our speakers on the call today are Pablo Legorreta, Founder and Chief Executive Officer; Jim Reddoch, EVP, Co-Head of Research and Investments and Chief Scientific Officer; Marshall Urist, EVP, Co-Head of Research and Investments; and Terry Coyne, EVP, Chief Financial Officer. Pablo will discuss the key highlights, after which Jim and Marshall will provide an update on our royalty portfolio and acquisitions. Terry will then review the financials. And after concluding remarks from Pablo, we will hold a Q&A session. Chris Hite, our Vice Chairman, will also join the Q&A session.

And with that, I'd like to turn the call over to Pablo.

Pablo Legorreta - *Royalty Pharma plc - Founder, Chairman of the Board & CEO*

Thank you, George, and welcome to everyone on the call. I am delighted to report another year of strong financial performance and strategic execution by Royalty Pharma. On Slide 6, I would like to begin by summarizing our many accomplishments in 2021, which underscore the robust momentum in our business. First, we delivered strong top line growth of 18% and bottom-line growth of 19% for 2021.

In addition, we strengthened our balance sheet through a $1.3 billion bond financing, which included a social bond, which reflects our commitment to corporate social responsibility. During the year, we were active in deploying capital with $3 billion in announced transactions across five deals, and we were well ahead of our target of $7 billion by 2025 that we communicated at the time of our IPO. In total, we've already announced approximately $5.9 billion of transactions since the beginning of 2020.

We continue to benefit from the competitive modes we have established over the past 25 years, and our business is as strong as ever. As a result, we remain the leader in the Royalty funding market in 2021 with a 50% share of transactions by value, based on our internal estimates. Importantly, we expect deals completed over 2020 and 2021 to contribute greater than $750 million to our top line in 2025 with potential for upside from development-stage therapies. We think this is an impressive number, and really highlights our unique ability to compound growth as we layer on additional royalties through value-enhancing acquisitions.

When we look at our portfolio, we also saw tremendous progress. We were -- we more than doubled the number of development-stage therapies in a single year, an aspect of our business model, which is truly unique in biopharma, in line with our track record of picking winners, especially compared with industry benchmarks. We're encouraged by the recent positive readouts for AstraZeneca's PT027 for asthma and Biohaven's zavegepant for migraine, and are optimistic that many of the positive clinical updates across our portfolio will ultimately lead to approvals and drive patient benefit.

On Slide 7, you can see our financials in a little more detail. In the fourth quarter, we delivered 12% growth an Adjusted Cash Receipts, our top line, and 15% growth in Adjusted Cash Flow, our bottom line. For the full year, as noted, we delivered growth of 18% at the top line and 19% at the bottom line. The strong double-digit momentum puts us in a tremendous position to deliver another year of strong financial performance in 2022, as Terry will speak to when he discusses our guidance.

Slide 8 shows our strong growth track record since our IPO in June 2020, which is a testament to the underlying power of our business. By leveraging our deep expertise, a leading position at the heart of funding life sciences innovation, we're able to consistently replenish our portfolio and drive compounding returns. This has allowed us to deliver seven consecutive quarters of double-digit bottom-line growth and very strong top line growth as well.

Importantly, in 2021, we digested the expiring HIV franchise royalties, our fourth largest source of royalties in 2020, which accounted for 13% of total royalty receipts and still delivered high teens top and bottom-line growth. This speaks to the strength and breadth of our existing portfolio and the momentum from our recent royalty transactions.

Slide 9 expands on this point. The strong performance of our base business was by far the primary driver of growth in 2021, and accounted for around 3/4 of our 18% top line growth. New transactions in 2021 added about 400 basis points to growth, largely from the addition of Tremfya, Cabometyx and OXLUMO. Royalty expires mainly on the HIV franchise, had a negative impact of 900 basis points, but were easily absorbed by the strength of our diversified portfolio. Of note, we achieved 14% organic growth from our existing portfolio, about double the growth rate we initially guided at the beginning of last year.

This is a great illustration of what makes Royalty Pharma a unique player in life sciences. Our proven ability to grow through losses of royalties and constantly diversify the portfolio with value-enhancing royalty acquisitions truly sets us apart from other biopharma companies. With that, I will hand over to Jim to update you on our royalty portfolio.

James Reddoch - *Royalty Pharma plc - Executive VP, Chief Scientific Officer and Co-Head of Research & Investments*

Thank you, Pablo, and hello, everyone. Today, I want to spend a couple of minutes updating you on the development of our portfolio in 2021. Slide 11 shows our transaction funnel over the past year. We've had a well-established sourcing, diligence and evaluation process that sees us execute only on what we believe to be the most promising opportunities. This has resulted in the excellent returns on investment we have generated since our founding.

In 2021, we reviewed over 300 potential transactions, resulting in around 85 signed confidentiality agreements and 33 proposals submitted. Our disciplined and highly selective approach resulted in us ultimately executing five transactions across 11 therapies or approximately 4% of those we initially reviewed for a total value of $3 billion, including $2.3 billion upfront.

Slide 12 shows the growth of our pipeline, and explains why we are running ahead of our capital deployment target of $7 billion to 2025, which we announced at the time of our IPO. Since 2019, the number of initial reviews conducted by the team has increased by around 50%. This reflects the increasing demands for capital to fund life science innovation and the strong capabilities of our research and investments team. Over the same period, the number of in-depth reviews we conducted has also increased over 50%. Following our diligence process, this has resulted in a greater than 1/3 increase in the value of transactions executed between 2019 and 2021. And as we stand today, our pipeline continues to present substantial opportunities and is highly active.

Please turn to Slide 13. Executing a clear strategy, we continue to broaden our portfolio. Over the past 2 years, we have announced transactions of $5.5 billion, bringing in a total of 20 unique therapies, eight of these therapies were development stage at the time of acquisition and nine are either currently or projected to be blockbusters based on consensus sales forecast through 2030. These new medicines span five therapeutic areas.

Unlike traditional biopharma companies, the strength of our business model is that we are agnostic to therapeutic categories and modalities. We evaluate each opportunity on a case-by-case basis so that we can quickly pivot our focus to areas where breakthrough medical innovations are happening. Importantly, these transactions are expected to add more than $750 million to our top line in 2025 using consensus estimates with potential upside from the development-stage therapies. For context, this compares with our Adjusted Cash Receipts for full year 2021 of $2.1 billion, and highlights our unique ability to consistently replenish our portfolio.

I will now turn it over to Marshall to discuss our royalty acquisitions.

Marshall Urist - *Royalty Pharma plc - Executive VP and Co-Head of Research & Investments*

Thanks, Jim, and good morning. As a reminder, two of our key strategic pillars are investing in royalties on both approved and development-stage therapies. Since 2012, around 55% of our investments have been in approved therapies while 45% have been in the development stage. If we look at the early performance of our recent transactions on Slide 15, the picture is very encouraging. Among the approved therapies we recently acquired, the majority have seen increases to Street consensus sales forecast since the acquisition date with more than half increasing by substantial double-digit percentages. We believe this reflects our careful assessment of the clinical and commercial opportunity during the diligence process.

The development-stage therapies in our portfolio have also progressed well, and many are expected to have pivotal readouts or regulatory decisions in the near future. Pablo mentioned earlier that our success rate here has exceeded industry benchmarks. In fact, we've invested close to $8 billion in development-stage therapies since 2012. Excluding therapies still in development, we have a 79% approval rate based on a number of investments, and a 95% approval rate based on the value of our investments.

Moving to Slide 16. Our overall market share in royalty transactions based on our internal estimates is around 60% over the past decade and nearly 90% in deals in the $500 million-plus range since our founding. This reflects our many years of experience in tailoring flexible, win-win funding solutions for our partners, our unique focus on biopharma, and our ability to do so at scale due to our deep access to capital.

This slide gives 2 examples of how we have joined a biotech partner in their growth journey, providing capital to launch new medicines and to fund the development of promising, innovative candidates through multiple transactions over time.

In the cases of BioCryst and Biohaven, their needs were different. But for each, we were able to provide timely solutions that enabled them to accelerate the process of bringing their innovation to patients, both in terms of supporting commercialization and in-pipeline progress. This has been recognized by the financial markets with strong share performance since we made our investments in rising consensus forecast for their rare disease and migraine therapy.

Slide 17 illustrates our latest example of tailoring solutions for our partner. In this case, Cytokinetics. Last month, we agreed to expand our long-standing partnership by providing up to $450 million in funding, in part to acquire royalty on aficamten, a potential new medicine for hypertrophic cardiomyopathy. This is a serious disease that impacts the lives of up to 100,000 people in the U.S. Our diligence was based on positive Phase II data, which indicates that aficamten has the potential to deliver significant patient benefit in blockbuster sales in a therapeutic area that has already seen significant M&A with Bristol's $13 billion acquisition of MyoKardia. Aficamten has breakthrough FDA designation and is planned to start pivotal trials this quarter.

Slide 18 highlights the expected clinical and regulatory events for our portfolio. In summary, 2022 looks to be a very milestone-rich year. Importantly, we anticipate Phase III results for a number of potentially transformative therapies, including Gilead's Trodelvy in third-line hormone receptor-positive metastatic breast cancer, results from Cabometyx in combination with IO, in renal, prostate and lung cancer; J&J's Tremfya in ulcerative colitis, and potentially seltorexant in depression; Roche's gantenerumab in Alzheimer's, BioHaven's oral migraine prevention therapies, zavegepant and GSK's otilimab in rheumatoid arthritis.

On the regulatory front, we would highlight a filing of PT027 in asthma in the first half of 2022, and a European regulatory decision on Biohaven's Vydura, the European brand name for rimegepant in migraine, which is Nurtec ODT in the U.S. Many of these milestones represent major commercial opportunities and could add significantly to our long-term growth outlook.

With that, let me hand over to Terry.

Terrance Coyne - *Royalty Pharma plc - Executive VP & CFO*

Thanks, Marshall. Let's move to Slide 20. Total royalty receipts grew 5% in the fourth quarter and 11% for full year 2021 versus the respective year-ago periods. Growth drivers in the fourth quarter included cystic fibrosis as well as payments from Biohaven, and our new royalty on Tremfya. For the full year, we also saw significant growth contributions from Promacta, Imbruvica and Tysabri. As Pablo described, these positive factors more than offset the loss of contribution from our legacy HIV franchise as the royalty term ended.

Slide 21 shows how our royalty receipts translated to strong Adjusted Cash Flow. As you're aware, Adjusted Cash Receipts is a key non-GAAP metric for us, which we arrive at after deducting non-controlling interests. This amounted to $543 million in the fourth quarter, growth of 12% compared with the year ago quarter. For the full year, Adjusted Cash Receipts were $2.1 billion, up 18%.

When we move down the column for each period, operating and professional costs equated to approximately 9% of Adjusted Cash Receipts, consistent with our 2021 guidance. Our operating and professional costs for 2021 were broadly similar to last year as 2020 included a number of one-time costs related to our restructuring, IPO and inaugural bond offering. Ongoing R&D funding payments remained at a low level. Net interest paid was de minimis in the fourth quarter, about $127 million for the full year 2021. This reflects the timing of the semiannual interest payments associated with our $6 billion unsecured note offering in 2020. As a reminder, these payments are in the first and third quarters of our financial year.

After other items, this resulted in Adjusted Cash Flow, our bottom line, of $488 million or $0.80 per share for the fourth quarter and $1.8 billion or $2.91 per share for the full year. For the full year, this translates to an Adjusted Cash Flow margin of 83%, which underscores the strong financial leverage in our business model. The higher Adjusted Cash Flow margin in the fourth quarter of 89.8% reflects the semiannual timing of interest payments that I just referenced.

On Slide 22, we continue to maintain our financial firepower. We deployed $2.6 billion of capital on royalty acquisitions during 2021 as well as $430 million -- $439 million on dividends and distributions. As a result, given our strong cash flow generation and proceeds from our bond issuance in

July, we added $2.1 billion of cash and marketable securities at the end of December, which is slightly above our position at the end of 2020. Our leverage stands at 2.6x EBITDA on a net basis and 3.7x EBITDA on a total basis. As a reminder, the average coupon on our debt is slightly above 2%, which compares with our target returns on Royalty acquisitions in the high-single digits to teens-percentage range. We believe this cost of capital is a durable competitive advantage for our business. We continue to feel very good about our ability to execute on our business plan and create value for shareholders. This confidence is reflected in the announcement last month of a 12% increase in our quarterly dividend.

My final slide provides our full year 2022 financial guidance. We expect Adjusted Cash Receipts to be in the range of $2.225 billion to $2.3 billion, an increase of approximately 5% to 8% over the $2.1 billion we delivered in 2021. This outlook reflects the expected strong underlying performance of our royalty portfolio, partially offset by the residual impact of the loss of royalties on the HIV franchise as well as the end of the DPP-IV royalty term in March, for which we will receive the last royalty receipts in the second quarter of 2022.

Importantly, and consistent with our standard practice, this guidance is based on our portfolio as of today and does not take into account any future royalty acquisitions. Our guidance is also based on today's FX rates. And we would note that if the U.S. dollar were to strengthen by 5% against the euro from current levels, we estimate this would result in a $15 million to $25 million headwind to our Adjusted Cash Receipts this year.

Turning to our operating cost ratio. We expect this to be approximately 9% of Adjusted Cash Receipts in 2022, which is similar to 2021. Net interest paid for full year 2022 is expected to be around $170 million, reflecting the net interest associated with the bond offering in July 2021, as I signaled on our third quarter earnings call.

With that, I would like to hand the call back to Pablo for his closing comments.

Pablo Legorreta - *Royalty Pharma plc - Founder, Chairman of the Board & CEO*

Thanks, Terry. Let me close by saying how pleased I am with our outstanding performance in 2021. And as you have seen from our guidance, we expect to deliver another strong year in 2022. If I take a longer-term perspective, Royalty Pharma plays a unique role at the heart of funding the golden age of life sciences innovation, and I truly believe our prospects have never looked better.

Our compelling business model and competitive advantages give us the potential to deliver attractive compounding growth over the long term. Slide 25 highlights one of the reasons that we're so excited about our future, namely the potential to partner with biotech companies on their growth journeys. The number of biotech IPOs has more than tripled since 2016. And this, coupled with significant innovation, is fueling an unprecedented need for capital in the industry.

Our research shows that today's unprofitable biopharma companies are expected to have more than $1 trillion in operating expenses over the next decade, layering in additional company formations will further increase the capital needs. This creates a massive opportunity set for Royalty Pharma, which we're confident we can execute against.

On Slide 26, my team and I would be delighted if you will join us for our Inaugural Investor Day, which we now have officially scheduled for May 17. We plan to include a detailed discussion of the outlook for royalty funding, our updated capital deployment objectives and our long-term growth targets. And of course, you will have plenty of opportunity to ask questions and interact with management.

With that, I would be happy to take your questions.

George Grofik - *Royalty Pharma plc - Senior VP and Head of IR & Communications*

We'll now open up the call to questions. Operator, please take the first question.

QUESTIONS AND ANSWERS

Operator

(Operator Instructions) Our first question comes from Geoff Meacham with Bank of America.

Geoffrey Christopher Meacham - *BofA Securities, Research Division - Research Analyst*

Just got a few. I want to get your thoughts on the current macro environment and its implications. So the first question is maybe for Terry. Does the pace of rate increases this year change your assumptions at all on things like deal flow or ratios? And then second question, I guess, for Pablo. You have so many recent IPOs that are trading at pretty low cash multiples and -- it's not clear whether the financing headwinds are really going to abate. And so does it make sense to shift to earlier stage? I know you guys have some risk guardrails, but the question is does lower valuation kind of outweigh the earlier stage of some of the more recent IPOs?

Pablo Legorreta - *Royalty Pharma plc - Founder, Chairman of the Board & CEO*

Sure. Terry?

Terrance Coyne - *Royalty Pharma plc - Executive VP & CFO*

Yes. So Geoff, in terms of the current macro environment, yes, I mean, we've been obviously watching, like everyone, the plans for rate increases this year and the potential impact on our business. I would say from Royalty Pharma's balance sheet perspective, we're very lucky that we locked in rates at pretty attractive times with a weighted average debt maturity of over a dozen years. And we have -- I think around 60% of our debt matures in 2030 and beyond, which is a very good position for us to be in.

In terms of how it could impact deal flow, I think it's -- we're seeing a lot of opportunities right now. I think this has been -- if anything, we kind of view it as accelerating a trend where companies are looking at royalties more and more as an attractive way to fund their businesses. And I think that the equity market backdrop certainly doesn't hurt that momentum as well. But these things take time. We're very happy with the level of the discussions in our pipeline. And hopefully, this can be a productive year and productive next couple of years.

Pablo Legorreta - *Royalty Pharma plc - Founder, Chairman of the Board & CEO*

So adding -- and adding to what Terry already provided, which is an interesting perspective on the macro environment. I think in terms of strategic focus going forward, you're not going to see a significant shift in us going into earlier-stage investments. But I'd like just to maybe share with you something we've communicated to you and our investors in the past, which is the fact that Royalty Pharma has always been very open-minded in the way we approach things.

We have told the team for decades, and that's really the way we approach things, that we have to come to a transaction with an open mind, not carrying any preconceived notions or ideas, essentially looking at sort of a blank piece of paper, sitting down with management teams, listening to their story, trying to understand the opportunity and then decide if it's something we want to get involved with or not.

And it may -- in some cases, it may include things that are maybe a bit earlier than what we have done in the past. I think from a big picture perspective, Geoff, a company, our company, which is deploying $2 billion to $3 billion per year. You've seen last year us deploying $3 billion, in the prior year, it was in excess of $2 billion. For us to actually make investments, small scale, that could be $50 million, $100 million in earlier stage products is totally appropriate, and we will probably do that in a way where we actually make an investment earlier, but with already an agreement with the company to actually fund the later-stage trials.

And so -- and we've done that already in one case in the past where we founded an earlier-stage trial, and there was a commitment for us, if certain milestones were met to actually fund the Phase III. And I think the other thing I'll mention is that there is no question that royalty funding has become mainstream. So you have that underlying very strong trends of growth, companies wanting to fund with Royalty. And obviously, as Terry pointed out, the current market conditions accelerate that.

So what you're also going to see at Royalty Pharma is us adding very selectively new members to our research and investments team and also a few people that are going to help us reach out to companies. And that's something that we're very excited to do in the next quarter or so.

Operator

Our next question comes from Umer Raffat with Evercore ISI.

Michael Gennaro DiFiore - *Evercore ISI Institutional Equities, Research Division - Equity Research Analyst*

This is Mike DiFiore in for Umer. Just one on gantenerumab. Prior to the NCD, I think you guys had said that gantenerumab could be a multibillion-dollar opportunity. So now in light of the DRA proposal, be great to get updated thinking here. Also, if you could offer any color on the potential royalty structure of brain shuttle gantenerumab? I know you said you couldn't, but if there's any update along those lines, that would be great.

Pablo Legorreta - *Royalty Pharma plc - Founder, Chairman of the Board & CEO*

Marshall, why don't you take this question?

Marshall Urist - *Royalty Pharma plc - Executive VP and Co-Head of Research & Investments*

Absolutely. Mike, thanks for the question. So two parts to that one. So on gantenerumab, we had -- we've discussed with you guys before that we think this has the potential to be a multibillion-dollar product. I don't think anything that we've seen in the NCD discussion is -- changes our view of that.

Just to take a step back, gantenerumab is exactly the kind of product that we think is a great part of the Royalty Pharma portfolio and, I think, came in with some of the -- through some of the themes that Pablo talked about in terms of helping companies solve their problems, and that's exactly what we did, and how gantenerumab joined the portfolio.

I think bigger picture, though, to answer your question, we still -- our original thesis around gantenerumab was that you had two well-designed trials that reflect sort of the best thinking on trial design or product profile and a marketer that could really make this a big product. I think you fast forward a year, 18 months from now when you've had readouts for gantenerumab, potentially other drugs in this class, I think the debate, the discussion is really going to be informed by the full picture of the safety and efficacy of these products once we have multiple consistent data sets out there. And I think that will ultimately drive the conversation long term.

So certainly, we're following all the developments with aduhelm with interest, but really, we want to see what this next crop of data shows, and we think that's ultimately going to determine what this class is going to be.

I think the second part of your question was just on brain shuttle. So brain shuttle is -- the brain shuttle gantenerumab is a product that is royalty-bearing under that agreement. And so it would ultimately be royalty-bearing to us. It is early, right? Like we've said, it is just entering, I think, a Phase II trial recently. So a long way to go there, but we'll be excited to have that potentially as part of the portfolio as well.

Operator

Our next question comes from Chris Schott with JPMorgan.

Christopher Thomas Schott - *JPMorgan Chase & Co, Research Division - Senior Analyst*

Just two for me. Just on overall capital deployment levels. They've obviously trended well above the ranges you gave at the time of IPO. Should we be thinking about this higher level of capital deployment? So let's say, the $3 billion we saw in 2021 as a new normal for Royalty? It seems like capital needs for the industry are up. You're able to diligence more than the past. So the answer may be yes there, but just interested in your thoughts.

And the second thing was just coming back to, I think, one of the slides you presented. I think you submitted 33 proposals last year. You executed five transactions. Just a little bit of color on the other 28. Were those companies or royalties being done with somebody else where these companies did an equity financing? Or is there an ability to revisit some of those transactions as we think about market conditions changing, and maybe a little bit more favorable valuation, or less favorable valuation additions for the sellers that might have existed last year. So just any color on that would be appreciated.

Pablo Legorreta - *Royalty Pharma plc - Founder, Chairman of the Board & CEO*

Of course. So Terry is going to answer the first question about the guidance on capital deployment. And I think Jim can talk about the deals we look at and why we don't do some of the deals that we analyze in detail.

Terrance Coyne - *Royalty Pharma plc - Executive VP & CFO*

So Chris, on the capital deployment question, we're -- we've been very encouraged by how we've been able -- the deals we've been able to do over the last couple of years. And certainly, we recognize that we're tracking well ahead of the guidance that we originally gave at the time of our IPO. This is -- it does tend to be something, and we tried to be really clear with investors.

It is uneven, and there's going to be years where we have significant capital deployment, and then there's going to be years where we're more patient and cash builds, and we wait for the right opportunities. And we've done that throughout our history. I would say though that to us, the market does feel a lot deeper now than it did 5 or 10 years ago. And I think that, that can create the opportunity for more consistent capital deployment. And we do feel like the levels that we've been deploying are very encouraging. We're going to really unpack this, I think, in greater detail at our Analyst Day in May. So I would just say stay tuned, and we'll try to really describe the opportunity at that event.

James Reddoch - *Royalty Pharma plc - Executive VP, Chief Scientific Officer and Co-Head of Research & Investments*

Chris, to address your question about sort of the -- what happens between the proposals and the executed number of transactions. It's pretty similar to years past where it's kind of three different groups of possibilities. One is that they're done by our competitors or another group. I would say that's in 2021 was a smaller number than it has been in the past. Another segment of that was times where we got into diligence, which -- sometimes it requires a proposal for us to see the deep diligence. And just we didn't get totally comfortable with the asset and the end after seeing the deep diligence.

And then the third group is just times where there hasn't been a transaction or hasn't been a transaction yet. So some of those are continuing because sometimes there's some need to have kind of a lead time to get to a transaction. So it's pretty similar to the groupings, that sort of transition from proposals submitted to executed transactions as we have seen in the past.

Operator

Our next question comes from Steve Scala with Cowen.

Stephen Michael Scala - *Cowen and Company, LLC, Research Division - MD & Senior Research Analyst*

I have two questions. One is mechanical and then one is bigger picture. So the mechanical question is, apparently, Royalty Pharma will not garner royalties on Januvia during its pediatric exclusivity in the second half of this year. Is this unique in this situation? Or is this how all of these similar situations are, and will be contracted? Or does the payment in the second half -- second quarter contemplate sales in the second half. So that's the mechanical question.

The bigger picture question is for Pablo. You have probably seen many tough markets for biotech companies in your career. How is this one similar to or different from past circumstances? Some commentators think there could be a sustained devaluation of biotech assets. If this were the case, then how would that impact your business? I could foresee opportunities, but I could also foresee risks.

Pablo Legorreta - *Royalty Pharma plc - Founder, Chairman of the Board & CEO*

Sure. Terry, do you want to take the first question?

Terrance Coyne - *Royalty Pharma plc - Executive VP & CFO*

Yes. So on the Januvia question, every contract and royalty that we acquire tends to be unique. There's certainly -- in many instances, we do end up being paid for pediatric exclusivity. But in the case of Januvia and Janumet, there was a hard cutoff date in the contract. And so that's why we kind of know with 100% certainty that it sort of ends in March, and our last payment will be in the second quarter.

Pablo Legorreta - *Royalty Pharma plc - Founder, Chairman of the Board & CEO*

Regarding the -- go ahead.

Stephen Michael Scala - *Cowen and Company, LLC, Research Division - MD & Senior Research Analyst*

Can I just follow up. So the patent actually ends in July. I actually don't know when in July. But will the payment -- or will the second quarter payment be through June or through -- when does that actually end?

Terrance Coyne - *Royalty Pharma plc - Executive VP & CFO*

Yes. So the second quarter payment will be based on royalties on sales through March. And so this is a -- this was a unique situation where there was a date in the contract.

Pablo Legorreta - *Royalty Pharma plc - Founder, Chairman of the Board & CEO*

Yes. Regarding your -- the other part of your question about downturns in the market. I mean this is honestly nothing new, and we have been through very significant downturns. I was actually looking recently at a graph of the biotech performance since 1997. And I think we've had four or five downturns in the market that have approached. And these downturns occur, over a period of like maybe a year, two years. Some -- I think there's one or two that have been more prolonged where it's 30% down. In one case, it was even 40% down. But I think there's some very, very strong underlying trend that we need to keep in mind.

And as a result of that, like since 1997, the biotech indexes are up 38x. So a multiple of 38, and the IRR is somewhere in the 17% to 20%, depending on what period you look at, which is just incredible growth. And I think what the point is that the long-term trend here is that there's been so many advances in our understanding of human biology, human health diseases that have opened up so many new approaches for innovation to actually end up solving or addressing unmet medical needs.

And that secular trend, I think, is going to be with us for many decades to come. And that's the thing to keep in mind that yes, it may be the case that now the market got ahead of itself with many companies that may -- were maybe early, went public and raised money. And -- but I think there's definitely going to be many, many, many of these companies that are going to survive, will get funded because they have just really cutting-edge approaches to address human disease.

And our job at Royalty Pharma is going to be to try to find those little gems that always exist in the space. And we're so excited about all of this -- of what I'm telling you now. And I think we're in a really good, very, very strong position to actually -- through the network we have, through the years of actually investing in life sciences, the fact that now we're more visible than we were in the past. The fact that now royalties are mainstream -- mainstream way of funding.

And I think that just bodes to a super promising future for Royalty Pharma. But thank you for the question. I think it's really interesting to reflect on the ups and downs of this really exciting industry biotech. But that's my perspective.

Operator

Our next question comes from Matthew Harrison with Morgan Stanley.

Chen Yuan Yang - *Morgan Stanley, Research Division - Research Associate*

This is Charlie on for Matthew. I have three questions. The first is which of the development-stage assets that you have, in your view, have the biggest discrepancy between your internal projections versus the Street projections? And then my second question is, can you remind us on the leverage ratio or the additional debt that you could potentially take on while still maintaining that investment-grade rating? And my final question is your expectation for the Bristol Myers' mavacamten label and the potential read-through to aficamten in terms of the market opportunity.

Pablo Legorreta - *Royalty Pharma plc - Founder, Chairman of the Board & CEO*

Yes. Sure. Marshall should answer the question. I think just from my own perspective, one that I'm very excited about is gantenerumab. And obviously, there's risk there, but it's also a product that can be very, very big, given the huge need for an effective treatment for one of the biggest problems that is affecting older people, Alzheimer's. So that's exciting to me. But Marshall, go ahead.

Marshall Urist - *Royalty Pharma plc - Executive VP and Co-Head of Research & Investments*

Sure. Charlie, I think about your question a little bit differently, which is part of the reason we covered this in the prepared remarks, which is just how we have really built an exciting development-stage portfolio. And I think if you look its prepared remarks on Slide 18, just from the deck, how interesting it is that 2022 is really seeing the cumulative effect of a lot of the additions to our portfolio over the last few years.

And while we're not necessarily focused on events like this as a core part of our business, I think as we continue to show disciplined growth in our development-stage portfolio, I think the result is that we hope to have a steady flow of the events we have this year. And I think the thing that's really striking and interesting about it is if you just look at the breadth of the type of events we have, different mechanisms, therapeutic areas, it's really incredibly broad when you take a step back and look at what the team has put together for all the milestones this year. So I think we are -- we're excited to see how this year plays out. And I think we'll continue to build the portfolio, and hopefully have more events like this in years to come.

On -- I think the second part of your question was on the mavacamten PDUFA date, and what the label looks like. Well, certainly probably a little early to comment on that. Bristol, I think, has expressed confidence in the product. Talked about $4 billion in unrisk-adjusted peak year sales. They seem excited to get this product launched and off the ground. We'll see the label when it comes out, and we can discuss it then.

But I think Importantly, like we talked about with aficamten, we think this is a really exciting new area. It's exciting to see targeted therapy and a new -- targeted therapy in cardiology and a new wave of innovation there, and we're excited about what the Cytokinetics team is going to do with aficamten. So I'll pass it to Terry for -- I think for the question on leverage.

Pablo Legorreta - *Royalty Pharma plc - Founder, Chairman of the Board & CEO*

Let me just add a perspective to the good answer that Marshall gave you, and this is on Slide 18, where we have the milestones. And I think if I look back over the last two decades and see what was going on with Royalty Pharma five years ago, 10 years ago, the slide would look very similar as what you're looking at today with so many different value drivers in our portfolio. In the past, there was obviously things like Humira getting approved for psoriasis or many other indications or Lyrica some of the HIV AIDS investments we had when it went from Truvada to Atripla and then to the quad.

But I think the point is that what this really tells you is what's so unique about Royalty Pharma that in a way that we're able to capture given the openness of our business model is really the best of biotech. We -- like a lot of investors are trying to find an attractive biotech company to invest. Guess what? We have within Royalty Pharma, some of the most exciting products of the industry with a lot of value drivers, milestones and also some of the big pharma products, right?

So I think it's interesting just to reflect on that. I always felt that as a public stock, we would differentiate ourselves because we would have constantly a lot of really good news flow that investors could look at and see if they could then make an attractive investment that was going to have significant value drivers. But Terry, go ahead.

Terrance Coyne - *Royalty Pharma plc - Executive VP & CFO*

Yes. So on the leverage question, we remain committed to our investment-grade credit rating. And so we finished the year with total debt-to-EBITDA of 3.7x. And we've operated in kind of this 3 to 4x band over the last 15 years. We're very comfortable operating in that band. We can go above four for the right acquisition where we see -- where we really see a clear path to delevering from there. So that's how we think about it. And I think we do feel like we have a lot of financial flexibility and firepower to take advantage of the opportunity that we see in front of us.

Operator

And we have a question from Greg Fraser with Truist Securities.

Gregory Daniel Fraser - *Truist Securities, Inc., Research Division - Research Analyst*

Great. You haven't updated your long-term growth outlook while you had a particularly strong year in 2021, and also exceeds your capital deployment target by a large margin. Is the long-term growth outlook still intact? Or is that something that you're waiting to update at the Investor Day? And then a quick question on 2022. Are there any notable milestone payments that are factored into the guidance range?

Terrance Coyne - *Royalty Pharma plc - Executive VP & CFO*

So I'll take those this. So in terms of the long-term growth outlook, that's something that we're going to update those sort of targets and our latest thinking at our Investor Day. And then in terms of this year, any milestones that factor into our guidance. The answer is no. We try to -- we would try to give you a heads up if we did see any one material onetime things. in there. And at this point, we don't see anything in our forecasts.

Operator

And I'm showing no further questions at this time. I'd like to turn the call back to Pablo Legorreta for closing remarks.

Pablo Legorreta - *Royalty Pharma plc - Founder, Chairman of the Board & CEO*

Sure. Thank you, operator, and thank you to everyone on the call for your continuing interest in Royalty Pharma. My team and I look forward to continuing to share our progress with you. If you have any follow-up questions, please feel free to reach out to George. And I will just say that we really hope to see all of you during our Inaugural Investor Day in May. Where we're going to be excited to share with you and really take a deeper dive in many of the topics that we've discussed today. So thank you again for your interest in Royalty Pharma, and hope to see you in May.

Operator

This concludes today's conference call. Thank you for participating. You may now disconnect.