NATERA JP MORGAN

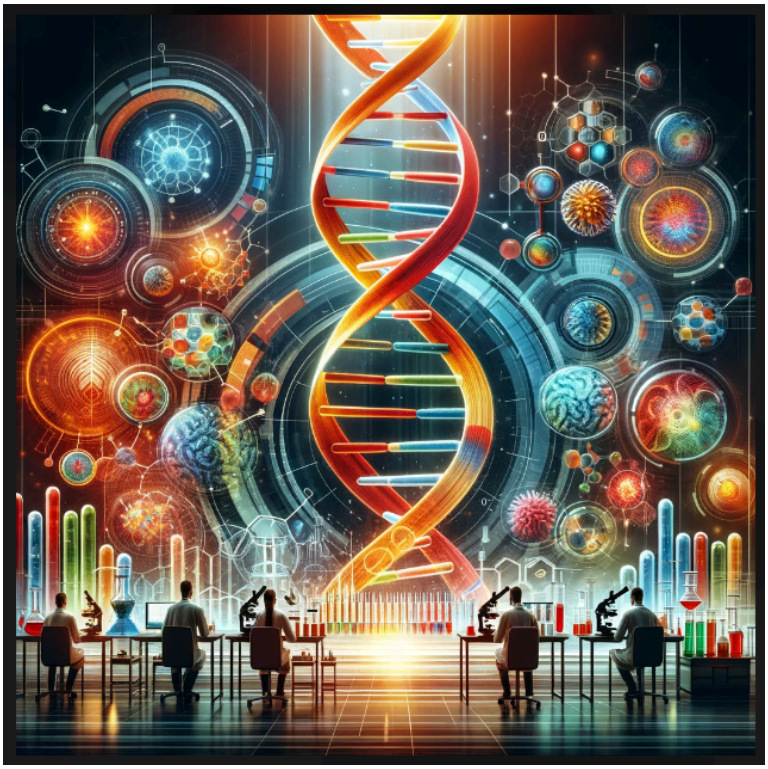
JANUARY 9, 2023

Audiofile and Deck were online, January 11.

https://investor.natera.com/events-and-presentations/default.aspx

A cloud copy of the PPT PDF is here (16pp):

https://drive.google.com/file/d/1JX_MJ6Ko-wCHGZOsJuZYnunuDx0kXOwy/view?usp=sharing



Natera Blog,
https://www.discoveriesinhealthpolicy.com/2024/01/natera-at-jp-morgan-big-lessons-on.html

Visual for same,
https://brucedocumentblog.blogspot.com/2024/01/visual-for-my-natera-blog-1-17-2024.html

**An AI summary follows.**

Based on the transcript of Natera's January 2023 presentation, the key points for a biotech investor are:

1. **Leadership in Cell-Free DNA Technology:** Natera leads in this space, with a focus on under-penetrated markets and strong market share in existing products.
2. **Innovative Approach:** Continuous innovation and technology development are highlighted, underpinning Natera's success in its fields.
3. **Financial Performance:** The company exceeded revenue guidance for 2023, showing strong growth and improved gross margin performance.
4. **Volume and ASP Momentum:** Significant growth in volume, driven by products like Signatera, and momentum in Average Sales Price (ASP) across the business.
5. **Strategy on Unprofitable Accounts:** Natera is moving away from unprofitable accounts towards a path to profitability.
6. **Rapid Path to Cashflow Breakeven:** The company is accelerating its timeline to achieve cashflow breakeven, indicating strong financial health.
7. **Market Leadership in Oncology:** Natera is a leader in **MRD** testing with significant market penetration and a large number of peer-reviewed publications.
8. **Innovation in Signatera:** Significant first-mover advantages in oncology, particularly with Signatera, backed by a strong patent portfolio and clinical data.
9. **Success in Market Access and Reimbursement:** Broad Medicare coverage across various cancers, with advantages in state biomarker laws and pricing.
10. **Women's Health Leadership:** Natera dominates in cell-free DNA and genetic testing in women's health, with a significant market share.
11. **Advantages in 22q Testing:** The company's differentiated approach in 22q testing provides a competitive edge.
12. **Expansion in Organ Health:** Growth in cell-free DNA products like Prospera and Renasight, indicating a potential future growth area.
13. **Future Catalysts:** Expectation of guideline inclusion in women's health, colorectal cancer trial readouts, and potential for expanded commercial coverage.
14. **Investment in R&D and Commercial Infrastructure:** Sustained investment in these areas is bearing fruit, with expectations of new product launches.
15. **Guideline Changes and Regulatory Approvals:** Potential changes in guidelines and regulatory approvals could significantly impact Natera's market and financial positions.

These points highlight Natera's market leadership, financial health, and strategic initiatives, particularly in the areas of reimbursement, ASP, and coverage by payors.

An **AI-written**, journalist-type summary follows.

*Natera, a prominent player in cell-free DNA technology, has shown remarkable leadership in under-penetrated markets, with a strong foothold in existing products. The company has exceeded its revenue guidance for 2023, indicating robust growth and improved gross margin performance.* ***Notably, Natera's volume and Average Sales Price (ASP) have seen significant momentum, especially in products like Signatera.***

***The company's strategic shift away from unprofitable accounts*** *towards profitability is noteworthy. This move, coupled with an accelerated timeline for achieving cash flow breakeven, underscores Natera's financial health. In oncology, Natera leads the market in* ***MRD*** *testing, backed by a solid patent portfolio and clinical data, particularly with Signatera.*

*Their success in market access and reimbursement, especially broad Medicare coverage across various cancers, positions them advantageously. Natera also dominates in women's health with its cell-free DNA and genetic testing, and its differentiated approach in 22q testing adds to its competitive edge. Expansion in organ health with products like Prospera and Renasight signals potential growth areas.*

*Upcoming catalysts, such as expected guideline inclusions, colorectal cancer trial readouts, and expanded commercial coverage, are poised to impact Natera's market position significantly. The company's sustained investment in R&D and commercial infrastructure, promising new product launches, and potential changes in guidelines and regulatory approvals, all indicate a strategic positioning for continued leadership in the genomics and oncology sectors.*

**Two journalists, Adam Bonislawski and Kelsy Ketchum of Genomeweb, summarized Natera's JPM pitch, in this way**. I've highlighted what they saw a key lessons, re reimbursement.

Natera

*CEO Steve Chapman expanded on Natera's preliminary Q4 and FY 2023 financial results, released Tuesday, noting* ***that revenue growth was driven largely by the Signatera minimal residual disease test [MOLDX LCD]****, which has reached "near-peak levels" of growth, as well as significant momentum in the average selling price (ASP) of its tests.*

*The firm is also on track to hit **cash flow breakeven** in 2024, he noted, and it reduced its annual cash burn by about $200 million in 2023.*

***Improving reimbursement has been a key focus for Natera, and the company has taken strides to boost test payments. It has improved its billing operations to further raise its ASP, Chapman said. "Just in the core business, without new guidelines coming in, without new Medicare coverage, without going and getting new commercial coverage, we're getting paid a higher percent of the time because we're operating better."***

***The firm has also made multiple submissions to Medicare's MolDx program to expand Signatera into further cancer indications that will hopefully boost reimbursement, said Solomon Moshkevich, the firm's president of clinical diagnostics. "These are areas where we're already doing a decent amount of testing commercially and just not collecting as much as we will after getting the approval," he said.***

*Chapman also discussed upcoming clinical trial results in 2024, noting that its randomized trial ALTAIR — the circulating tumor DNA-guided treatment escalation arm of the **CIRCULATE-Japan trial evaluating Signatera's utility in colorectal cancer patient**s — is expected to read out in the first half of the year and will potentially be a catalyst for growth. If the readout is positive**, it may also positively impact reimbursement, Moshkevich added.***

***State biomarker laws will also likely have an effect on payments and reimbursement. Multiple states have enacted mandates for commercial payors to cover biomarker testing if it is covered by Medicare. About 60 percent of Signatera's volume is provided to beneficiaries covered by commercial payors but much of that testing is not getting reimbursed, which would change under the biomarker laws. Those changes could lead to Signatera's ASP doubling, although Natera's model is conservative because "we haven't seen this play out before," Chapman said.***

*Other potential catalysts **include commercial payor coverage** for the Prospera test for kidney transplant assessment; **guideline inclusion** of the firm's women's health tests, possibly for 22q11.2 deletion testing or carrier screening; and product launches across its core business and new areas.*

*Chapman emphasized the innovation of its noninvasive prenatal test (NIPT) Panorama to screen for 22q11.2 deletion syndrome, which is an area of focus for the company. Panorama uses SNP-based technology to target a very small region of the genome in cell-free DNA, which Chapman said makes it able to get more than 25 times the read count at the particular region of interest than tests that use massively parallel sequencing.*

*In the firm's Microdeletion and Aneuploidy Registry (SMART) trial, Panorama was performed on more than 20,000 patients, 12 of whom had a fetus with confirmed 22q11.2 deletion syndrome, and Panorama detected 10 of these cases (83.3 percent sensitivity) with a positive predictive value of nearly 53 percent. Results were published in the American Journal of Obstetrics and Gynecology in 2022, and at the end of 2022,* ***the American College of Medical Genetics and Genomics conditionally recommended that noninvasive prenatal screening for 22q11.2 deletions be offered to all patients.***

*The company is also expecting the initial readout of performance data for its early cancer detection test in 2024. Depending on the results, it will consider starting a clinical trial in 2025 or 2026 to support a US Food and Drug Administration submission, Chapman said.*

*Chapman also briefly addressed Natera's patent infringement victories in 2023, including a permanent injunction against Invitae and ArcherDx and a preliminary injunction against NeoGenomics. Chapman said that it is challenging to get injunctions and that they speak to the strength of Natera's intellectual property*.

The following section highlights reimbursement from the subsequent transcript:

**We've been very successful in market access and reimbursement.** We've gotten broad **Medicare** coverage now across colorectal, bladder, breast and pan-cancer immunotherapy monitoring.

That [MEDICARE COVERAGE] actually become even more valuable now with these biomarker laws that have gone in place in states now that are covering more than 50% of the population in the United States. Those laws that are now in place or have been voted on and been approved state that, if you have Medicare coverage, that commercial payers are obligated to pay. So the fact that we have this broad Medicare coverage puts us at a significant advantage going forward.

We also have a unique status, which is the Advanced Diagnostic Laboratory Test designation, and that's allowed us to get pricing on the clinical lab fee schedule of **$3,500 per recurrence monitoring** Signatera test. Now, there's **one other competitor** that has a tumor-informed test that's been priced on the clinical lab fee schedule and their rate is **$795**. So this ADLT is a very big differentiator and, in fact, the price point for 2025 has already been determined as well and the price will be back at **$3,900 in 2025**.

The final area where we think we have a significant **first-mover advantage is all the infrastructure** and the experience that we've built since 2019. We now have a very fast turnaround time. We have an extensive network of mobile phlebotomists. We have patient portals that we've launched, we have physician portals, we have EMR connectivity with Epic and many other EMR systems, and we have a large team of folks that collects the tissue in a very fast manner so that we can run the test and deliver the results back to the patient. We scaled up our labs and we've also built out an extensive commercial team, which is very expensive to build out. We pre-built the commercial and medical affairs and customer service team so that we could service the future volume, and now we're in a position where we can take on more volume without rapidly increasing our operating expenses as we scale up.

**TRANSCRIPT**

steve chapman:

Thanks for coming. I'm Steve Chapman. I'm the CEO of Natera. That's Solomon Moshkevich, the president of Clinical Diagnostics, and Mike Brophy, our chief financial officer. So this is the standard safe

harbor statement. Natera today is the leader in cell-free DNA technology. We're addressing three very large under-penetrated markets. We performed more than 10 million tests across 12 different products. We have approximately 175 peer-reviewed publications. We have more than 400 patents. We have slightly more than 3000 employees. We launched our first cell-free DNA test in 2013, Panorama, in cell-free fetal DNA testing. And when we launched, we were the fourth company to market. Today we have about 50% market share and we're very clearly the market leader based on the strength of our technology. In 2019, we took that same technology and we expanded it into oncology and organ health, which I'll talk about in a minute.

So what was it that made us successful? We think it is the focus on these four critical areas. We take leading-edge technology, but we don't stop there. We constantly innovate. We're on version seven or eight now of Panorama. We're launching new versions of Signatera, this constant focus on innovation that sits alongside a platform of leading technology. We have broad and talented commercial teams. We have extreme focus on excellent customer and patient experience, and we're a leader in peer-reviewed published data.

I'm excited today and this morning, I guess we wrote this out largely already, but I'm excited to tell you about our results for Q4 and for 2023. We had an incredible quarter and an incredible year. We finished 2023 about $20 million above the top end of our revenue guide. And, as a reminder, throughout the course of last year, we already raised revenue guidance three times throughout the course of the year, so we had a very strong Q4 revenue growth. It was approximately 38%, year-on-year, and this is driven from strong ramp in Signatera, significant ASP momentum across the business and very strong gross margin performance in Q4. And we're going to be reading out our gross margin performance on our earnings call in early February, but again, very strong gross margin performance.

I'll also just say, for all of these numbers that we're reading out, units, revenue, we're giving conservative estimates. The final numbers will be read out on our earnings call. On the volume side, we had very strong and continued volume momentum. This was driven largely by Signatera volume continuing to grow. We had an excellent sequential growth quarter, actually near peak levels in our Signatera growth, which was excellent and in line with our expectations.

When you look at the remainder of the business, we came in roughly similar to where we were in Q3, and that's basically expected when you look back historically at the performance of the business over time. In years where we're not having a competitor like Semaphore or Progenity go out of business, you see Q4 is pretty similar to Q3 and that's sort of where we ended up this year. Now, we also have, at the same time, a strategy to move away from some unprofitable accounts or accounts where we don't see a path to profitability. And if you look at our revenue growth and you look at our improving gross margin and you look at our rapid path to cashflow breakeven, I would say that that strategy is working very well.

Before we leave volume, I want to say, particularly in women's health, in December we had a record level of volume per receiving day. So again, we're really pleased with how things finished up and the trajectory that we have going into 2024. Now I want to spend a little bit on cash burn. We are on a rapid path to hitting cashflow breakeven. Our goal for a long time has been to hit a cashflow breakeven quarter in 2024, and I'm pleased to say that we're actually accelerating that timeline.

When you look at our cash burn for Q4, the total number was 60 million, but that includes $27 million of prepayments where we were able to negotiate deals to bring CapEx spending from 2024 into December of 2023, roughly, and get an additional 20% discount on top of our already discounted supply agreements. So we thought that was a good trade-off, but netting that out, the cash burn would've been

in the range of $33 million. So again, we're on an accelerated path. We're seeing things go faster than we had expected and we're reinforcing the fact that we're going to hit a cashflow breakeven quarter in 2024.

I want to spend a minute on oncology. **Natera is today the market leader in MRD testing. We think this is about a $20 billion TAM opportunity. We have more than 60 peer-reviewed publications covering our MRD technology. Last quarter in Q4 more than 35% of oncologists in the United States ordered an MRD test from Natera. We performed more than 300,000 tests last year**. And again, remember these are conservative numbers. We have more than 150,000 patients in our clinical genomic database and we have more than 400 dedicated sales, customer service, patient service and medical affairs employees that are just dedicated to the oncology force alone.

Now, I want to take a step back and just talk for a second about what is Signatera. So, with Signatera, we do tissue sequencing and then we make a personalized test that is just for you, just for the patient, and we use this test to look at positive or negative results to inform adjuvant treatment decision-making, to detect cancer recurrence. Is your cancer coming back? And then also to look at whether your therapy is working or not. The test is available in a pan-cancer setting and has been validated across a pan-cancer setting. And we have significant first-mover advantages in Signatera.

The first is in innovation. We have more than 220 oncology-specific patents that support our MRD test. The second is in clinical data. Today we have more than 60 peer-reviewed papers covering Signatera and we have multiple randomized trials underway. Some of these were started more than five years ago and are now getting ready to read out. In fact, we expect to have the first results of our colorectal randomized trial, the ALTAIR study, in 2024, which we're really excited about.

**We've been very successful in market access and reimbursement. We've gotten broad Medicare coverage now** across colorectal, bladder, breast and pan-cancer immunotherapy monitoring. That's actually become even more valuable now with these biomarker laws that have gone in place in states now that are covering more than 50% of the population in the United States. Those laws that are now in place or have been voted on and been approved state that, if you have Medicare coverage, that commercial payers are obligated to pay. So the fact that we have this broad Medicare coverage puts us at a significant advantage going forward.

We also have a unique status, which is the Advanced Diagnostic Laboratory Test designation, and that's allowed us to get pricing on the clinical lab fee schedule of $3,500 per recurrence monitoring Signatera test. Now, there's one other competitor that has a tumor-informed test that's been priced on the clinical lab fee schedule and their rate is $795. So this ADLT is a very big differentiator and, in fact, the price point for 2025 has already been determined as well and the price will be back at $3,900 in 2025.

The final area where we think we have a significant first-mover advantage is all the infrastructure and the experience that we've built since 2019. We now have a very fast turnaround time. We have an extensive network of mobile phlebotomists. We have patient portals that we've launched, we have physician portals, we have EMR connectivity with Epic and many other EMR systems, and we have a large team of folks that collects the tissue in a very fast manner so that we can run the test and deliver the results back to the patient. We scaled up our labs and we've also built out an extensive commercial team, which is very expensive to build out. We pre-built the commercial and medical affairs and customer service team so that we could service the future volume, and now we're in a position where we can take on more volume without rapidly increasing our operating expenses as we scale up.

In women's health, we are the market leader in cell-free DNA and, broadly, the market leader in women's health genetic testing. We have a suite of products on the market. We think the TAM here is about $10 billion. We have more than 85 peer-reviewed publications that have studied more than two

million patients. We perform more than **five million NIPT** tests and today in the United States, when someone orders an NIPT, one out of two of those tests is performed by Natera.

I want to take a second to talk about **22q** because that's one of the hot areas right now in this space, and that's an area that we've talked a lot about. Natera's 22q test is highly differentiated, and as 22q is studied more and in the future as this goes into societal guidelines and becomes commonplace, the unique differentiation that Natera has in its 22q test is going to become more and more and more valuable.

When we run our test, we're using a SNP-based technology that allows us to target this very small region of the genome, which is around two and a half to three megabases. So for companies that are doing massively parallel sequencing, they have to sequence the entire genome multiple times in order to get the correct depth of read. So we think when we're doing targeted sequencing, we can actually get more than 25 times the read count at the particular region of interest that companies that are doing massively parallel sequencing can. And this is a very significant advantage that translates into excellent clinical performance.

So from a clinical performance standpoint, we studied our test in the SMART trial, which was a seven-year multi-site prospective study that enrolled more than 20,000 patients. 87.6% of those patients had a complete genetic outcome, which is not where we just observed the baby at birth or we asked the doctor, "Well, did you think they were positive?" We actually did a genetic microarray on the newborn babies or on an amnio or CVS to confirm for all positives and negatives, or 87% of the positives and negatives, what the actual genetic outcome was for that child.

And so what we saw was striking. The incidence of the disorder was very high, about **1 in 1,500 pregnancies, which is in line with Down syndrome** for women under the age of 28. We also saw that we had an extremely high sensitivity. So overall our sensitivity was 83%, but that included the small deletions that are less than 2.5 megabases. When **most companies report out their sensitivity**, a lot of the massively parallel sequencing companies, they're only talking about the 2.5 megabase deletion and bigger. They're completely **ignoring deletions** that are below 2.5 megabases, and that makes up 41% of the disease load. So imagine if you're doing a screening test where your total available opportunity, even if you add 100% sensitivity, is to detect 59% of the affected patient population.

We don't think that that's a good test. So in this study we showed 83% sensitivity overall for any 22q deletion, but we showed 95% sensitivity for the deletions above 2.5 megabases. We had an excellent positive predicted value of greater than 50%, which we think is really stellar. Now, recently, you've heard some of the other laboratories talk about how they have 100% positive predicted value or they come out and they put out slides and they say, "Well, we're better than Natera. We have 100% positive predicted value."

Well, you'll notice that they don't report out their sensitivity. So you have to wonder, well, why are they only talking about their positive predictive value, but they're not talking about their sensitivity? That would raise a red flag for me. And what we've seen in some of the papers that are out is that the massively parallel sequencing companies we believe have a sensitivity that's in the range of around 25%. So just keep that in mind when you see other companies talking about how great their positive predicted value is.

So finally, on clinical utility, we think screening for 22q is very important. Early intervention can improve outcomes. We can detect cardiac anomalies. We can try to treat hypocalcemia at birth. This has now been validated, the actionability of screening in a prenatal diagnosis article, and in fact this is already

recommended screening by ACMG and we look forward to ACOG recommending 22q in the future if that's something that they choose to do.

**Now I want to move to organ health for a minute. Across the organ health business, we have our cell-free DNA product line, which is Prospera for kidney, heart and lung.** And there we have more than 50% of transplant centers working with Natera, and we've published now more than 30 peer-reviewed publications across those different products. Then we also have our chronic kidney disease testing line, which is our **genetic screening product, Renasight**. Incredibly, one in seven US adults has chronic kidney disease, or somewhere in the range of 35 to 40 million patients in the United States.

Already, about 55% of nephrologists in the United States have ordered the Renasight product. So we think this is potentially a very big opportunity in the future. Now, when we first identified this opportunity in 2019, we decided, like we normally do, we would set up a prospective multi-site study to determine what the incidence of the disorder was or of these genetic disorders were in the chronic kidney disease population and also whether there was clinical utility of screening, whether, if a doctor got a result back and they showed their chronic kidney disease patient was positive, would they make an intervention?

Well, incredibly, what we found is that one in five chronic kidney disease patients had a positive genetic finding. That's one of the highest incidences of positivity in any population cohort, but, incredibly, one out of two of those positives received a new diagnosis or reclassified diagnosis as a result of their screening test with Renasight. And one in three of the patients that were positive actually had a change to the physical therapy and treatment that they were receiving. So this is extremely high clinical utility. This is roughly in line or maybe better than what's observed generally for hereditary cancer testing, which is now mainstream, and we think this is going to be a very large opportunity in the future.

I'll just finish up before we open up Q&A talking about potential catalysts. Natera today has very strong revenue growth, driven by strong and improving average selling prices. We're on track for cashflow break-even in a particular quarter in 2024 without any additional catalyst, just running the core strategy of the business. Now, we think that's important because we're getting the cashflow break-even the right way. We didn't have to mortgage the future of the company, cut back our R&D efforts, really trim back our commercial or lab footprint.

So we have right now peak R&D spending and peak commercial footprint out in the field that's going to go support our core product lines over the next several years. And this significant historical investment in innovation is actually coming to fruition now. We're starting to see the results of all the investments that we've made in R&D and building this commercial infrastructure. And so we have these big catalysts now that are going to start to hit in 2024 in areas where we've made significant investments over the last several years.

The first is guideline inclusion in women's health. We think it's possible we could see a 22q guideline. In addition, we think we could see some carrier screening guidelines. I know that's been talked about, so we're excited about that opportunity. We're well positioned to, I think, to help patients in those two areas. We also expect to have the first readout of our randomized trial in colorectal cancer. This is the ALTAIR study, which we think will read out in the first half of 2024. We're also excited about the opportunity to get commercial coverage for Signatera and Prospera with these new biomarker bills.

**There's a state mandate that covers 50% of the US population that, if Medicare covers the test, that it has to be covered by commercial payers**. Today, that's not in our model at all. That should be coming in soon, and we think that that's an opportunity. We're starting on that right now. And, in addition, as we

mentioned on our last call, we have exciting product launches coming, things that we've been working on for a long time, across the core business in women's health, in ecology and organ health and in new areas beyond. So, with that, we'll open it up for Q&A.

Rachel:

Perfect. Thank you, Steve. So I wanted to just start it off here by talking about the 4Q pre-announcement, obviously another healthy beat relative to expectations. I was curious, could you walk us through what drove the strength in the quarter? When we look a bit closer, it looks like volume was sequentially down, quarter-over-quarter, in 4Q, versus that typical 4Q seasonality that you see where it's typically higher. So can you talk about some of that spread between the volume growth versus the revenue growth? Was there any one-timers that played into that dynamic as well?

steve chapman:

Yeah. I mean, first, volume wasn't down, just to clarify. As we said, we report out conservative numbers and so what's on the slide versus the reality is we actually did really well**. I think we did see volume improvements in ASP, strong Signatera growth. I think it's just that core execution of the business is what's driving the revenue beat.**

**We've been saying for a long time that we think there's some improvements in the average selling price that we can hit just by turning the crank and improving the billing operations.**

I've personally been working on that, along with Mike and others for now over a year, and so we're starting to see just in the core business, **without new guidelines coming in, without new Medicare coverage, without going and getting new commercial coverage, we're just getting paid a higher percent of the time because we're operating better. Then, with that, we're seeing improvements in Medicare Advantage and I think all this is leading to increased revenue**. Mike, you want to add anything to that?

Mike Brophy:

No, I think that was good.

Rachel:

Perfect. Then maybe just digging into some of the volume by quarter, can you help us think about how was Signatera versus women's health contributing in the quarter and then specifically within Signatera, how much of that contribution was from the clinical side on volumes there? You noted some of that strong sequential quarterly growth in Signatera, but any color there would be helpful.

Mike Brophy:

You want me take that?

steve chapman:

Yeah, sure.

Mike Brophy:

Look, on Signatera volumes, I think across the board, we had a very healthy quarter and we'll give the full detail on the Q4 call. But that includes good, strong sequential volume growth on the clinical side, and we also had a healthy quarter on the pharma side, as you might expect for Q4 year-end, as well.

Rachel:

Perfect. And then just looking at 2024 and potential range of outcomes there, you had noted that for this year, volume growth came in at around 20%. During 3Q, you had noted that you could see a potential similar volume unit growth number for this year. Does that still hold true in terms of your outlook for 2024, and then walk us through, just given that comp dynamic, that plays out as well.

steve chapman:

Yeah, I mean, I'll just say we're in three very large opportunities that at least two of the three are largely under-penetrated and in women's health there's still a long way to go. So I think there's a big opportunity ahead of us and, like I said in the presentation, we're seeing very strong quarter-on-quarter sequential growth in Signatera. I think it was near record levels of sequential growth and then in women's health and the remainder of the business, I think a record December when it comes to units per receiving day. So we have a lot of good momentum going into 2024.

In addition to that, I think we've got a lot to look forward to. As these guidelines come into place, our differentiation gets larger and larger in women's health. Our 22q product is highly unique and that's something that we're going to be focusing on. In addition to that, we have multiple suite of product launches that are going to be coming this year that we're excited about and we're continuing to build on our moat in Signatera.

Rachel:

Perfect. Then maybe just on new products, today you didn't share a ton on new products, but you did mention at the end there that we can expect some exciting update in the future, kind of teasing that we could see some of the core business but also beyond, so curious, what could that mean? Any other details there right now would be helpful.

steve chapman:

Yeah, I mean, when you look across our portfolio, one of the things that we've done really well is continue to innovate and I think we plan to do that same thing across women's health. We're excited about new launches that are coming across organ health. We have great opportunities there. And then particularly in oncology supporting Signatera and surrounding Signatera, we expect to have exciting new launches.

Rachel:

Perfect. Then just talking about some of the screening and some of the data here, further, you said that you were expecting some of the screening data based on your prior commentary, so when could we expect that and then maybe walk us through some of the other data readouts that you're excited for this year, outside of ALTAIR?

steve chapman:

Yeah, we're excited about actually reading out the performance data from our early cancer detection strategy. What we've said is we're going to spend around maybe 10 to $15 million this year, and then, based on the data readouts, we'll look at kicking off an FDA-enabling trial in 2025 and 2026. So we have two datasets, advanced adenoma and colorectal cancer. I think we've run one of those and we're in the process of running and analyzing the second one, and then we'll be doing the initial readout, which I think will be followed by some additional readouts later this year, and then we'll make a decision what we want to do there.

Rachel:

Helpful. **Maybe just looking at ASP improvement across the portfolio, that's been a key theme, not only in Signatera but also in women's health, which is impressive given the maturity of the market there. So you've talked about some of your investments, and billing operation improvement being a key factor there, but can you elaborate on exactly what that's entailed and then how much further runway is there on that front to improve that ASP growth**?

steve chapman:

Yeah, I mean, I'll just give you an example. I think one of the areas where it's difficult to... Even if you have a **covered service, sometimes you don't get paid by the insurance company, and I think everybody in diagnostics deals with this. Maybe the insurance company asks for medical records and that process of going back to the doctor and getting a copy of the chart** or getting the medical records, something along that way ends up dropping or not getting executed and then they say, "Look, hey, it's clear it's a covered service. We have an NIPT policy for low risk. This patient's low risk, but we're not going to pay you because you never went and returned back the medical records." I think there's different things like that where we can do a better job and we've spent the last 12 months really looking at what those are and how we can make improvements on those, and we're starting now to put some of those in place and we're seeing improvements.

Rachel:

Helpful. Then maybe shifting over to cash burn and some areas on the P&L, obviously you've had the top line expansion, but you've also done pretty nice on the gross margin line improvement as well, so can you elaborate on some of those improvements you've made on gross margins, some of the workflow adjustments and new platform migrations as well, and then what's left to do on that gross margin line to help you achieve that cashflow break even?

steve chapman:

Yeah. **So we're improving the average selling price and we've seen that now across all the different areas of the business. The ASP is going up.** That's the number one thing. Then, second, we're reducing the cost of goods sold and that comes from a suite of activities. Some of it is our R&D budget being applied towards versioning sequencers or moving to new sequencing platforms or automating aspects of workflows that weren't previously automated, running certain tests like the tissue in our new laboratory versus using other means, and so a portion of the cost savings comes from that.

Another portion comes from just doing better on vendor negotiations, and that's something we've put a lot of energy on. In the vast majority of cases there's multiple suppliers that provide the similar type of tool that we're using, and so I think we've got a lot of ground from that as well. We do have, I would say, very significant COGS projects that are going to be hitting in Q1, sorry, the end of Q1 in the women's

health business, and then in Q3 and spread throughout the second half of the year. These are R&D projects that are going to be hitting.

Rachel:

Got it. That's helpful. Then maybe I just want to touch on some of the recent litigations. You've had a few wins in terms of patent litigation, especially on the oncology side, so I wanted to ask, how do you think about this when it comes to your competitive mode, given some of the preliminary injunctions that you've received?

steve chapman:

It's obviously very challenging to get a preliminary injunction or a permanent injunction, and so we think this speaks a lot to the strength of our intellectual property. We have more than 220 pending or issued patents just in the field of oncology, and so we think this puts us in a great position.

Rachel:

Perfect. Helpful. **Maybe shifting over to oncology then, just on ASPs for Signatera. On the ramp to get over $1,000 dollars on ASPs by the end of 2024**, can you talk about how much does that really hinge on some of the additional Medicare coverage that you have talked about today? Last time you'd spoke, you'd said that there was additional submissions coming in 2024, so how should we think about the puts and takes there?

steve chapman:

Yeah, so I would say it doesn't really hinge on that at all, and we can get over 1,000 just by turning the crank on the operations, but we have a lot of opportunity to actually do even better than that and maybe, Solomon or Mike, you guys want to comment on that further?

Solomon Moshkevich:

Sure. So, to Steve's point, there's a few different additional levers that can lead to further upside besides just the optimization on billing operations. First of all, we have multiple submissions in right now with Maldi-X that can further expand our covered indications in cancer. These are areas where we're already doing a decent amount of testing commercially and just not collecting as much as we will after getting the approval. Mike, do you want to add anything to that?

Mike Brophy:

Yeah. No, I mean, I think Medicare Advantage continuing to improve the fraction of time we get paid for coverage services from MA and also from traditional fee-for-service Medicare. Steve gave you an example with medical records, that's a pretty good heuristic. I mean, just making sure we've got the right information for the right patient at the right time. I think that's really all you need to do in order to drive the number above 1,000 at this point.

Solomon Moshkevich:

If I could add one more thing, I think, while we don't need guidelines changed to continue to execute on the strategy that Steve already outlined, we do look forward to a pretty significant catalyst, mid-2024,

with the ALTAIR trial reading out, and if that reads out positively, that would definitely have a positive impact on reimbursement and therefore on ASP as well as adoption.

Rachel:

Got it. That's helpful. **Maybe just shifting over then to the state biomarker bills, you've talked about in a bold case scenario, you could potentially see as much as a 20% plus improvement in ASPs from the bills by the end of 2024.** So, to clarify, are those positive impacts and the potential from some of these biomarker bills going into effect this year included in your ASP assumptions, or is that even more upside from here?

steve chapman:

Yeah, its upside. We're excited about that. I mean, look, what, 50%, maybe more, maybe 55% of our Signatera volume is commercial, and I think it actually might even be more like 60-

Mike Brophy:

Yeah, 60.

steve chapman:

Sorry, 60. **60% of our Signatera volume is commercial and largely we're not getting paid** on that volume today.

**So I think there are some cases where we're getting paid, but it's incredible. We've never been in this position before in diagnostics, where 50% of the patients in the United States are now covered by a state mandate that, if Medicare covers the test, the commercial payers have to cover the test. That's not in our model at all, but it's in the law, covering 50% of the patients in the United States. New York just voted I think the week after Christmas. Texas, California, these are all in place.**

So I think there's a process where we have to go get that executed, but if you consider 60% of the volume that we're getting is commercial, these laws are in place. We just have to go now and execute on that. I mean, that's a huge opportunity. We could see the ASP double. Now, we're not putting that in our model. We're talking about a 100 buck increase or something in that range, but there is this enormous opportunity. We're just being conservative because we haven't seen this play out before, nobody has, and I think we have to see how it goes.

Mike Brophy:

I think just generally, I think just the clinical utility that we've already shown with Signatera, I think just makes it inevitable that we're going to get broad commercial coverage for Signatera. And this is going to be one of the factors that potentially accelerates that process, and then we look forward to making more progress as well.

Rachel:

Got it. That's helpful. Maybe just on the upfront exome workflows, can you spend a minute talking about how that lowers the COGS profile and then why should we be excited about that launching in **San Carlos and then the Austin Labs as well?**

steve chapman:

Yeah. A very significant portion of our upfront exome workflows today are run at Natera's facilities, and we do use a handful of partners, as well, for part of our capacity or for excess capacity where we've built strong relationships and we've vetted high quality. I think, over time, it makes sense for us to be running more and more of that in our laboratory, and we've said that we will be doing that largely, I think, throughout the course of 2024.

Rachel:

Helpful. And then maybe shifting over to women's health here, just on ACOG and the potential for some guideline changes from there. First up, just in carrier screening, as carrier screening stands, now you've talked about ASPs in that 400 to $415 range, so where could those go if ACOG endorsed broad-panel carrier screening?

steve chapman:

Do you want to answer that?

Mike Brophy:

Yeah. I mean, look, historically the carrier screening book of business on a blended basis had ASPs in the 500 to 550 range. We saw that trail down quite significantly to the range that you mentioned, Rachel, really in the second half of 2022. Since then, we've actually seen some encouraging sequential improvement in the carrier screening reimbursement, and I think that would be further helped by a clear guideline if we were able to get that. So I think conservatively one could estimate that we could at least return to that 500 to 550 level for carrier screening, which is very important to this business. Just as a reminder, for every 100 NIPTs that we run, we run roughly 55 carrier screening tests, so a very significant opportunity for us to continue to drive that business.

Rachel:

Helpful. Then maybe just on 22q and microdeletions there, you mentioned ACMG. Can you talk about how ACOG and when's the latest in terms of your timeline expectations for that potential guideline change, and how does the positive endorsement by ACMG give you conviction in that as well?

steve chapman:

Right. We're not involved in any of the ACOG meetings or in working with ACOG, but what we can do is look back and say, "Did we deliver a clinical trial that was well-designed that had the right outcomes that are needed?" Does the clinical utility meet the bar for coverage from these major societies? And we think that it does. Now, Natera, I think, will benefit in a couple of different ways. I think the first is that we're highly differentiated on our 22q product, as I've described. **Massively parallel sequencing and SNP sequencing for 22q are very different and the big prospective study that's been done, the only large prospective study that's been done, is <u>on SNP-based</u> sequencing for 22q**.

So **I think there's some questions around whether payers are even going to cover in the future, the massively parallel sequencing versions**, we'll have to see how that plays out. But whether or not coverage is impacted for those that haven't done these extensive validation studies we have, there's very significant clinical performance differentiators. So we think we'll benefit from that, from the volume standpoint. And then generally, today, doctors want this test and we're running the test, but we're just

not getting paid on it. So this will help us, I think, get to a position where we're moving towards profitability where we can help more and more patients over time.

Rachel:

Got it. And then just sticking on that 22q topic, where do you see ASPs shaking out if you were to get positive guideline inclusion? You've mentioned that the Medicare rate is around $700, so how would you advise us to really model that 22q from an ASP standpoint?

steve chapman:

I think we're going to have to see where it pans out. Like you said, the clinical lab fee schedule's in that kind of 750 range, and we'll have to see from there where it goes.

Rachel:

Helpful. Maybe shifting over to organ health, then. You've talked a lot about the opportunity in kidney and the positive renal care results, but stepping back, can you talk about the current penetration estimates for cell-free DNA used in kidney transplant rejection monitoring, and then, in your view, what are the main challenges to increasing those penetration rates above current levels?

steve chapman:

We think it's maybe high single-digit, low double-digit penetration today, and I think, reading out some of these big clinical trials that have been underway for a long time is really what's going to be needed to move the needle. So we're excited that the ProActive study data, the initial readout from ProActive was released at a major conference this last summer, and that's now in submission for publication. And the results there were very strong. What we showed is that an increase in donor-derived cell-free DNA occurs up to four months in advance of rejection, and we think that's the exact type of data that societies and doctors are looking for. So we're looking forward to that reading out.

And then in heart and lung, we also have nice studies underway that are reading out. I look forward, one of them, the DTRT study, I think, has been accepted recently or is about to be, so that should be read out. It's a long way to go there, but I think the more exciting opportunity's in chronic kidney disease over time, I guess the bigger opportunity I would say.

Rachel:

Perfect. That's helpful. Maybe in the last minute and a half here, could you just highlight what do you think is the most underappreciated area of Natera's story, for investors?

steve chapman:

Well, I think we've kind of laid everything out here now, but I think as well as we've done, the fact that we're still in these very under-penetrated markets, I think can sometimes be easy to miss. I mean, Signatera, oncology, that $20 billion TAM, we're still in the very, very early stages, single-digit penetration, and we built an enormous mode here that I think is going to be very difficult for others to come in and be successful at the scale that we've been. So I think just maybe the leadership position that we're in and the breadth of the opportunity ahead of us.

Rachel:

Perfect. And with that, we're out of time. Thank you so much for joining us today. Thank you, everyone.

steve chapman:
Thank you. Thank you, [inaudible 00:39:12].

This is an alternate AI summary (Otter.ai)

# 20240109 natera jpm

## Summary

- **Natera's Q4 and 2023 results, focusing on revenue growth and technology innovation.** 0:05
    - Natera is the leader in cell-free DNA technology, with 50% market share in fetal DNA testing and expanding into oncology.
    - Speaker 1: Q4 revenue grew 38% YoY, driven by strong ASP momentum and gross margin performance.
- **Q4 performance, cash burn, and market leadership in MRD testing.** 3:18
    - Company expects to reach cash flow breakeven in 2024, accelerating original timeline.
    - Terra's MRD test is a $20B market opportunity with 60+ peer-reviewed publications and 35% of oncologists ordering in Q4.
- **Cancer diagnostics and personalized medicine.** 7:18
    - Company expects to release results of colorectal cancer trial in 2024, with broad Medicare coverage and unique pricing advantage.
    - Natera has a large team of collectors and labs to quickly provide test results to patients, with a market leader position in cell-free DNA and women's health genetic testing.
    - Natera's 22 Q test is highly differentiated and will become more valuable as it becomes commonplace, offering excellent clinical performance in a targeted sequencing approach with more than 25 times the read count at a particular region of interest compared to massively parallel sequencing.
- **Prenatal genetic testing and its clinical utility.** 11:34
    - Speaker 1: 87.6% of patients had complete genetic outcome, with 95% sensitivity for deletions above 2.5 Mega bases.
    - Sensitivity of massively parallel sequencing companies is around 25%, while they focus on positive predictive value.
    - Speaker 1 highlights the clinical utility of screening for genetic disorders in chronic kidney disease patients, with one in five patients testing positive and one in two receiving a new diagnosis or treatment change as a result.
    - The speaker notes that this is a significant opportunity for genetic testing in nephrology, with high incidence of positivity and clinical utility similar to hereditary cancer testing.
- **Natera's Q3 earnings and future growth opportunities.** 16:33
    - Natera is on track for cash flow breakeven in 2024 without cutting back on R&D or commercial efforts.
    - The company is well-positioned for significant catalysts in 2024, including guideline inclusion in women's health and a potential readout of a randomized trial in colorectal cancer.

    - Speaker 1 highlights the company's strong execution and improved billing operations as the main drivers of revenue growth, with volume growth down quarter over quarter but ASPs strong.
    - Speaker 4 provides additional color on Signatera volumes, noting sequential quarterly growth on both the clinical and pharma sides, with a healthy quarter overall.
- **Business growth, new products, and cost savings.** 22:07
    - Speaker 1 highlights momentum in women's health, including record December units per receiving day and upcoming product launches.
    - Speaker 1 and 2 discuss potential new product launches, including in oncology and billing operation improvement contributing to ASP growth.
    - Speaker 1 highlights challenges in getting paid by insurance companies, despite having covered services, due to issues with medical records and other processes.
    - Speaker 1 and Speaker 2 discuss improvements made to gross margin, including increasing average selling price and reducing cost of goods sold through R&D investments, vendor negotiations, and automation of workflows.
- **Diagnostic test reimbursement and potential growth opportunities.** 27:36
    - Speaker 1 highlights the company's strength in patent litigation, with over 220 pending or issued patents in the field of oncology.
    - Speaker 3 discusses additional levers for further upside, including multiple submissions for expanded covered indications in cancer and improving Medicare Advantage reimbursement rates.
    - Speaker 4: Clinical utility of Signatera makes commercial coverage inevitable, potentially accelerating the process.
    - Speaker 1: **60% of signature volume is commercial, with state mandates** covering 50% of US patients, creating a huge opportunity for ASP increase.
- **Genetic testing, reimbursement, and clinical utility.** 32:26
    - Speaker 4: Expects carrier screening reimbursement to return to pre-pandemic levels with ACOG guideline change (500-550 range).
    - Speaker 2: Encouraged by sequential improvement in carrier screening reimbursement, potential for guideline change to drive business growth.
    - Company believes positive guideline inclusion for 22 Q could lead to increased reimbursement rates, potentially exceeding $700 per test.
    - Speaker 1 highlights the under-penetration of cell-free DNA testing in kidney transplant rejection monitoring, with single-digit penetration rates in some markets.
    - Speaker 1 emphasizes the leadership position of their company in this area, with a broad opportunity ahead.