

Guardant Health Inc.(Q4 2022 Results)

February 23, 2023

Corporate Speakers:

- Alex Kleban; Guardant Health; VP, IR
- Helmy Eltoukhy; Guardant Health; Co-Founder, Co-CEO & Chairman
- AmirAli Talasaz; Guardant Health; Co-CEO & Director
- Mike Bell; Guardant Health; CFO

Participants:

- Dan Arias; Stifel; Analyst
- Max Masucci; Cowen and Company; Analyst
- Tejas Savant; Morgan Stanley; Analyst
- Derik De Bruin; BofA Securities; MD of Equity Research
- Jack Meehan; Nephron Research; Analyst
- Ruizhi Qin; JPMorgan; Analyst
- Puneet Souda; SVB Securities; Analyst
- Matt Sykes; Goldman Sachs; Analyst
- Dan Leonard; Crédit Suisse; Analyst
- Patrick Donnelly; Citigroup; Analyst

PRESENTATION

Operator^ Thank you for standing by. Welcome to the Guardant Health Fourth Quarter and Full Year 2022 Financial Results Call. (Operator Instructions)

I'll now turn the call over to Alex Kleban. Alex, please go ahead.

Alex Kleban^ Thank you. Earlier today Guardant Health released financial results for the quarter and year ended December 31, 2022.

Joining me today from Guardant are Helmy Eltoukhy, Co-CEO; AmirAli Talasaz, Co-CEO; and Mike Bell, Chief Financial Officer.

Before we begin I'd like to remind you that during this call, management will make forward-looking statements within the meaning of federal securities laws.

These statements involve material risks and uncertainties that could cause actual results or events to materially differ from those anticipated.

Additional information regarding these risks and uncertainties appears in the section entitled forward-looking statements in the press release Guardant issued today.

For a more complete list and description, please see the risk factors section of the company's annual report on Form 10-K for the year ended December 31, 2022 and in its other filings with the Securities and Exchange Commission.

This call will also include a discussion of certain financial measures that are not calculated in accordance with GAAP.

Reconciliations to the most directly comparable GAAP financial measure may be found in today's earnings release submitted to the SEC.

Except as required by law, Guardant disclaims any intention or obligation to update or revise any financial projections or forward-looking statements, whether because of new information, future events or otherwise.

This conference call contains time-sensitive information and is accurate only as of the live broadcast, February 23, 2023.

With that, I'd like to turn the call over to Helmy.

Helmy Eltoukhy^ Thanks, Alex. Good afternoon. Thank you for joining our fourth quarter and full year 2022 earnings call. I will start off our call today by providing an update on our progress over 2022 and go into more detail across our oncology business. I will then turn the call over to AmirAli for an update on our screening business. And finally, Mike will provide a more detailed look at our financials and outlook for 2023. Throughout the year, we made significant progress in each area of our business, as noted on Slide 3. Indeed, 2022 was a pivotal year for Guardant whereby we brought to fruition, our vision of revolutionizing three significant areas of unmet need in cancer care, therapy selection, recurrence monitoring and now screening.

Our current position in just one of these areas would be quite enviable. But to be positioned today, where we are defining a new standard of care for advanced cancer patients, cancer survivors and for average risk individuals with a portfolio of breakthrough tests is truly exciting. I am so proud of our team's dedication and commitment to our mission of using the data from our powerful blood tests to help patients across all stages of cancer live longer and healthier lives.

Building on this, I'm excited to share our first story related to the detection of an ESR1 mutation in breast cancer, just weeks after receiving FDA approval of Guardant360 CDx for ORSERDU. A breast cancer patient in her 50s that had undergone 2 successful rounds of treatment, but unfortunately, she had another occurrence earlier this year. She had become symptomatic with cancer having spread to the liver and spine, the patient without of therapeutic options.

Her doctor ordered Guardant360, which in only 7 days detected a number of tumor mutations but no historically targetable alterations. However, one of these [affected]

mutations is an emerging critical marker, ESR1. ESR1 mutations are present in up to 40% of ER-positive HER2-negative advanced breast cancers. This finding enabled the patient to qualify for treatment with ORSERDU, the first ESR1 targeted therapy.

With this targeted treatment, the patient now has the chance to attend her son's wedding this spring, one of her greatest wishes (inaudible), being able to impact patients' lives in this way is what motivates all of us here at Guardant.

Now turning to our performance on Slide 4. We are pleased with our strong finish to the year. We ended the fourth quarter with \$127 million in revenue, bringing our full year revenue to \$450 million representing growth of 20% over the prior year.

Moving on to Slide 5. Clinical test volume reached over 36,000 tests in the fourth quarter, up 41% compared to the prior year quarter and fueled by increased depth of ordering of Guardant360. This resulted in 26% year-over-year growth in clinical revenue in the fourth quarter, which was led by Guardant360 with increasing contribution from new products.

Turning to Slide 6. I'm more excited than ever about the growing potential of our Guardant360 franchise. We are still in the early days of building this \$10 billion therapy selection market, with less than half of newly diagnosed metastatic patients receiving some form of comprehensive genomic profiling. Guardant360 is established liquid biopsy leader with more than 2 of every 3 non-small cell lung cancer liquid biopsy tests being Guardant360.

In fact, over the past year, despite new entrants in the field, we have continued to maintain, if not expanded, our market share. Our hundreds of publications, CDx approvals and best-in-class commercial team have proven to be high competitive barriers. Progress continues for Guardant360 with a number of significant milestones recently, including our first approval for Guardant360 CDx to be used as a companion diagnostic for breast cancer alongside a first-of-its-kind treatment in patients with ESR1 mutations.

Following this approval, we are already seeing a positive impact in clinical volumes, expanded reimbursement across the portfolio with more than 250 million covered lives after recent UnitedHealthcare coverage for lung and breast cancer and the introduction of Guardant Galaxy, our AI-enabled, tissue-based testing platform to enhance the portfolio and accelerate biomarker discovery.

Importantly, Galaxy has shown an over 20% improvement in PD-L1 detection. We think this will further accelerate the gains we are making in the tissue market. As we look ahead to 2023, we have multiple drivers fueling our strong growth trajectory as we approach breakeven in our therapy selection business. These drivers include deployment of EMR integrations with customers as we continue to streamline ordering through our partnership with Epic, expected reimbursement in Japan later this year and the expanded utility and comprehensiveness of our therapy selection portfolio.

Turning to Slide 7. One of the key differentiators of Guardant360 CDx is the strength and breadth of our companion diagnostic offering. We now have 7 regulatory approved companion diagnostics covering a range of therapies, biomarkers and tumor types in both the U.S. and Japan. Global sales of the therapeutics where we have CDx coverage are expected to surpass \$35 billion in 2022.

Building on our success in lung cancer, we recently received our first CDx approval in breast cancer in the U.S., and we have [approval to] both KEYTRUDA in solid tumors and OPDIVO in metastatic colorectal cancer in Japan. The value of our efforts and investments over the years is becoming apparent as payers such as UnitedHealthcare increasingly expect CDx approval to gain coverage and our biopharma partners look to entrust increasingly critical CDx programs with established independent players with strong track records.

Moving to Biopharma on Slide 8. We finished the quarter with record volumes up 24% year-over-year. We have over 150 partners supporting our growth. Guardant Infinity from our Smart Liquid Biopsy platform now represents over 20% of our volume mix. Despite the strong growth in 2022, we now expect to see the impact to biopharma budgets from the inflation reduction act and a more restrictive funding environment for our smaller biopharma partners, which has led to delays and cost pressures not seen in many years.

Because of these pressures, we conservatively expect low double-digit growth for biopharma test volumes in 2023. That said, we do not expect these near-term headwinds to dampen the longer-term structural growth of our biopharma business with a steady trend towards more biomarker-driven therapies. Our Infinity platform ramp and the opening of a large market opportunity in China, all forming the foundation for further growth in 2024 and beyond.

Now shifting gears to Guardant Reveal on Slide 9. Our MRD franchise is in its second year post launch and is growing rapidly with 250% year-over-year growth in 2022. Guardant is the only company in the market with a clinically validated tissue free MRD asset. With our industry-leading turnaround time, existing commercial infrastructure and strong growth in CRC patients in 2022, we are just scratching the surface of this \$20 billion opportunity.

In 2023, we expect growth to be driven by increasing traction in key tumor types, including CRC, breast and lung and the technology upgrade to our smart liquid biopsy platform. We are also making great progress in a number of our clinical studies designed to demonstrate the power of our platform for patients in the adjuvant and residual disease settings. Recent clinical results from our TRACC Part B study showed 92% negative predictive value and greater than 2-year residual disease-free survival in ctDNA-negative patients supporting chemotherapy avoidance.

Based on these exciting results, the study is expanding significantly into TRACC Part C, which will include more than 1,600 patients. The trial will evaluate the use of ctDNA to

guide chemotherapy treatment decisions following surgery for Stage II/III CRC patients based on test results for MRD with Reveal. The study holds the potential to improve patient care and quality of life by reducing unnecessary use of chemotherapy through MRD. We are also making excellent progress in Pegasus and COSMOS but we look to have results from the latter part of this year or through the early next.

Overall, we had a substantial year of development across all aspects of our business, and 2023 is off to a great start. Our efforts towards payer coverage, customer relationships, clinical partnerships and technology upgrades will fuel our growth in oncology for years to come. I will now turn the call over to AmirAli to provide an update on our screening business.

AmirAli Talasaz^ Thank you, Helmy. Turning to Slide 10. 2022 was an exciting year for our screening business with the pinnacle being our ECLIPSE trial readout. In ECLIPSE, Shield demonstrated 83% sensitivity in detecting individuals with CRC with 90% specificity. Moreover, with our LDT test, we are seeing adherence rates of over 90% in the first 10,000 patients compared to just 43% adherence for Fit in the real-world setting.

We believe these results may be criteria need to obtain FDA approval, Medicare coverage, guideline recommendation and to become a preferred CRC screening option for millions of patients. The true effectiveness of the screening test is driven by both clinical sensitivity and the rate at which the testing modalities are completed. When individuals do not (inaudible) colonoscopy or stool tests, more cancers remain undetected.

The effective sensitivity of our [test and FIT] are 75% and 30%, respectively. As a reminder, for CRC detection indication, we expect to complete our PMA submission for FDA approval this quarter and anticipate FDA approval and launch of Shield IVD in 2024. We expect to receive Medicare coverage, obtain ADLT status and get included in ACS guidelines following FDA approval. We expect Shield Medicare ADLT pricing to be \$895 with a blended ASP of approximately \$500 ahead of private payer coverage.

Turning to Slide 11. As we shared at the JPMorgan conference in January, we've been receiving overwhelmingly positive feedback from the top leaders and patient advocates. These leaders understand the unmet need, the importance of adherence in completing a test and believe the observed sensitivity was above the bar. These leaders foresee the beginning of a new era in the cancer screening field with the disruptive blood testing modality.

Now turning to Slide 12. We've often said the best step is the test that gets done. As shown in this graph, the effective sensitivity of Shield in detecting cancer is higher than all other modalities of CRC screening. As a result, adding Shield as a testing option will increase overall screening compliance and result in potentially saving millions of life years over the current standard of care.

Moving on to Slide 13. We recently announced the initiation of a prospective study, U-Screen in partnership with the University of Chicago that will examine whether Shield improves overall CRC screening in medically underserved populations. This study will enroll up to 2,400 patients who have failed to complete the CRC screening tests. The evidence from prospective studies like this, in combination with our observed real-world adherence rate will support USPSTF guideline inclusion for Shield. In summary, I'm excited about the future of Shield and the beginning of the new era in the cancer screening field.

With that, I will now turn the call over to Mike for more detail on our financials and outlook for 2023.

Mike Bell^ Thanks, AmirAli. Turning to Slide 15 to review our financial results. Total revenue for the fourth quarter of 2022 was \$126.9 million, up 17% from \$108.1 million in the prior year quarter. Total precision oncology testing revenue for the fourth quarter was \$113.8 million, increasing 28% compared to \$88.7 million in the prior year quarter. This increase was driven by year-over-year growth in both clinical and biopharma sample volumes.

Precision oncology revenue from clinical tests was \$83.7 million, up 13% from \$64.2 million for the prior year quarter. Fourth quarter clinical test volume was 36,000, an increase of 41% from the same period of the prior year and an increase of approximately 3,600 tests from the previous quarter. This increase was driven by strong Guardant360 growth as well as increasing contribution from our new products, Reveal, TissueNext and Response.

For the fourth quarter of 2022, Guardant360 ASP was in the range of \$2,600 to \$2,700, consistent with the last few quarters. The blended clinical ASP was approximately \$2,320. As we have previously stated, the blended clinical ASP will continue to be influenced by both the volume mix of Guardant360 and the new products as well as the reimbursement amounts received for new products.

Precision oncology revenue from biopharma tests in the fourth quarter totaled \$30.1 million, up 23% from \$24.5 million in the prior year quarter. Biopharma test volume was strong with the fourth quarter totaling 8,200 tests, up 24% from the prior year quarter. Biopharma ASP in the fourth quarter was approximately \$3,670. Development Services and other revenue in the fourth quarter totaled \$13.1 million, down 33% from the prior year quarter, primarily due to a onetime catch-up royalty payment that was received in the fourth quarter of 2021, which increased the comparison base.

Gross profit for the fourth quarter of 2022 was \$79.8 million compared to a gross profit of \$74.7 million in the same period of the prior year. Gross margin continues to be in line with our mid-60s target coming in at 63% compared to 69% in the prior year quarter. The main driver of this change was the year-over-year difference in fourth quarter royalty revenue, as just mentioned.

Operating expenses for the fourth quarter of 2022 were \$225.9 million, an increase of 31% compared to \$172.9 million in the fourth quarter of 2021. Net loss was \$139.9 million or \$1.36 per share for the fourth quarter 2022 compared to \$90.9 million or \$0.89 per share in the fourth quarter of 2021.

Turning to the full year. Total revenue was \$449.5 million, up 20% from \$373.7 million in the prior year. Precision Oncology revenue increased 29% to \$392.0 million and was comprised of clinical testing revenue of [\$298.1] million, which grew 26% year-over-year and biopharma testing revenue of \$94.0 million, which increased 38% year-over-year.

Clinical test volumes for the year grew to 124,800, up 42% year-over-year from 87,600 tests. The blended clinical ASP was approximately \$2,400 for 2022, which was lower than the blended clinical ASP of \$2,700 in 2021. While the ASP for Guardant360 has been consistently in the range of \$2,600 to \$2,700 since mid-2021, the change in the blended ASP was due to both lower cash true-ups in 2022 versus 2021, and the change in mix between Guardant360, REVEAL, TissueNext and [Response]. Biopharma testing volume increased 40% year-over-year to 26,000 tests. Biopharma ASP in the full year was approximately \$3,610 slightly down from approximately \$3,650 in the prior year due to changes in product and customer mix.

Development Services and other revenues declined 17% to \$57.5 million in 2022, primarily due to the variable timing of progress and milestones related to projects with third parties. Gross margin for the full year 2022 was 65% compared to 67% in 2021. Operating expenses for the full year 2022 were \$837.6 million, an increase of 27% compared to \$661.7 million in 2021. Net loss was \$654.6 million compared to \$405.7 million in 2021. Net loss per share was \$6.41 in 2022 as compared to \$4.00 in 2021.

Moving on to non-GAAP financial measures on Slide 16. Non-GAAP operating expenses exclude stock-based compensation and related employer payroll tax payments, amortization of intangible assets and contingent consideration. Non-GAAP operating expenses for the fourth quarter of 2022 were \$201.2 million, a 37% increase from \$146.2 million in the prior year quarter. This increase was primarily driven by the investments made over the past 12 months across both our oncology and screening businesses, primarily in our commercial infrastructure and the continued development of our product pipeline and clinical data.

Non-GAAP net loss was \$119.6 million or \$1.17 per share for the fourth quarter of 2022 compared to \$70.4 million or \$0.69 per share for the fourth quarter of 2021. Adjusted EBITDA was a loss of \$109.8 million in the fourth quarter of 2022 compared to \$64.6 million loss in the fourth quarter of 2021. We define adjusted EBITDA as non-GAAP net loss adjusted for interest, income tax, depreciation, amortization and other income and expense.

Non-GAAP operating expenses for the full year 2022 was \$736.6 million, a 45% increase from \$506.8 million in the prior year quarter. Non-GAAP net loss was \$435.4 million for

2022 as compared to \$251.7 million for the corresponding prior year period. Non-GAAP net loss per share was \$4.26 for 2022 as compared to \$2.48 for the corresponding prior year period.

Adjusted EBITDA was a loss of \$403.4 million in 2022 compared to a loss of \$231.5 million in 2021. We ended the year with approximately \$1 billion in cash, cash equivalents and marketable debt securities, reflecting approximately \$600 million in cash used that primarily consisted of a free cash outflow of \$387 million and a onetime payments totaling \$192 million related to the purchase of our EMEA joint venture.

Turning now to Slide 16. In 2023, we will continue investing to maximize the very large opportunities in front of us. but will take actions to lower our operating expenses below 2022 levels, reduce our cash flow to \$350 million and extend our cash run rate beyond 3 years. 2022 was our peak year in terms of cash burn as we completed significant investments to establish what we believe is the strongest platform in oncology diagnostics. We can now start gaining material leverage as our infrastructure is firmly in place to support our core operations, research and development activities and commercial organization.

In addition, we have begun to implement operational efficiencies across all areas of our business, including the recent reduction of our workforce by 7%, translating to approximately \$25 million in annualized savings. For our Therapy Selection business in 2023, we will continue to aggressively target Guardant360 revenue growth, both in the U.S. and abroad, while simultaneously remaining on track to be breakeven in about 12 months' time.

In 2023, MRD spend will continue to be focused on clinical data development for reimbursement and increasing our market penetration. For screening, we will continue with select market development activities as well as continuing technical and data development for lung and other cancers while reserving the necessary resources to fund a strong commercial launch in CRC following FDA approval.

Now turning to our outlook for the full year 2023 on Slide 17. We expect full year 2023 revenue to be in the range of \$525 million to \$540 million, representing growth of approximately 17% to 20% compared to 2022. The key driver of revenue growth will be precision oncology, which we expect to grow by more than 20% over 2022. Clinical volumes are expected to increase by more than 35% with all products continuing to drive this growth.

Clinical ASPs will continue to be dependent on product mix with potential upside from additional commercial coverage for Guardant360 and TissueNext and (inaudible) reimbursement for Response. While we continue to expand our biopharma partnerships, we conservatively expect our biopharma volume growth to be in the low double digits, resulting from the impact of reduced biopharma budgets from the inflation Reduction Act and the more restrictive funding environment for our smaller biopharma partners. We expect development services and other revenue to be above \$50 million in 2023, with

quarterly revenue dependent on the signing and ramp-up of new partnerships, the timing of existing project milestones and the amount of royalty revenue received.

Finally, as previously discussed, we expect 2023 operating expenses to be below full year 2022, and free cash outflow to improve to \$350 million in 2023 and to further improve in the following years. This represents a significant departure from previous expectations and reflects our increased focus on operating expenses and cash burn.

And finally, turning to Slide 18. Our long-term vision is to transform cancer diagnostics through cutting-edge technology, a focus on high-impact opportunities and consistent execution. At this point, we will now open the call to questions.

QUESTIONS AND ANSWERS

Operator^ (Operator Instructions) Our first question comes from the line of Dan Arias with Stifel.

Dan Arias^ Helmy, or maybe Mike, on MRD and just Helmy commented on increasing contributions from new tests, anything you can help us with just in terms of Reveal assumptions underneath the revenue guide for 2023? And then as you think about the Reveal reimbursement process, I'm just curious whether it feels like CMS is getting more familiar with performance and data and the differences between assay types in a way that makes coverage decision time lines short for you guys? In other words, do you think the time between the payers coverage decisions for breast and the one that you presumably get for REVEAL can be shorter than what you saw for colorectal cancer?

Helmy Eltoukhy^ Yes. So I'll start there. I'll start with the second part. I mean, yes, I think certainly, when you have something disruptive like we have, which is a tissue free assay that I think is ultimately has [product market] fit in this market. It's also harder to understand and get your head around. It's a more advanced technology in many ways. But we went through a lot of, I think, that back and forth in that education, I think, in getting to where we are with CRC.

So I think we are fairly optimistic that as we have subsequent data sets supporting additional indications, that we'll be able to -- we'll be able to go through that process in a more timely fashion. The other thing I'll add is that we increased -- we're very excited about the progress we've made with Brazil. I mean I think we're going from almost insignificant revenue in '21 or '22 to something that is going to be in the low double-digit millions in '23. And so we're seeing that sort of engine really kick on just like we saw with 360 when we started. And so this is going to be a big business for us and one that ultimately, we believe, will be in a [pole] position for.

Operator^ The next question comes from the line of Max Masucci with Cowen.

Max Masucci^ Congrats on another year of great progress. So I was going to ask, just looking at the ramp we've seen for some competitive MRD test. I would imagine the

range for Reveal CRC revenue contributions could be quite wide. So I was just curious maybe how you're accounting for that? And then more generally, it would be great to hear how you rank order the key factors that will determine your ability to meet the \$350 million free cash outflow guide.

Helmy Eltoukhy^ Mike.

Mike Bell^ Yes, sure. I think on the real size, yes. I mean really, we'll see Reveal drives the volumes, I think, more than the revenue this year because of the reimbursement that we get, which is currently just from -- really from Medicare, and it's in the CRC adjuvant setting. And so I think we're still driving volumes in the CRC surveillance setting. And also, we launched in breast and lung last year, and we've seen really good traction there. So I think that feeds into our clinical volume growth, which we said is going to be over 35% in 2023.

And as Helmy just mentioned, it's going to start to drive some of that revenue growth, but that's going to take longer to come and it's going to be dependent on reimbursement. And then from the drivers from the free cash flow reduction, I mean, obviously, the increase in revenue that we'll see this year and the gross margins that we see, which we still expect to be in the 60s this year. It's going to help with the gross profit. And then we've talked about managing our OpEx to levels lower than in 2022.

And so if we can do that, if we can achieve the revenue, the gross margins and absolutely, we can manage the operating expenses and we've taken actions already to do that, then that's going to drive that reduction in free cash flow. And obviously, we've mentioned a few times that we've built out now a lot of the infrastructure within Guardant. And so it's now to us to really leverage that across the operations, R&D and the sales and marketing side. And even on our CapEx spend, which has been in the sort of \$70 million level for the last couple of years, that's going to significantly come down in 2023.

Operator^ The next question comes from the line of Tejas Savant with Morgan Stanley.

Tejas Savant^ Thanks for the time. So I'll ask a 2-parter, one on and one on screening. So starting with MRD, perhaps Helmy or Mike, could you chime in on how you think about the balance between this near-term revenue generation and cost control versus expanding into newer indications and priming the market ahead of getting reimbursement and making a bigger push.

And then on the ECLIPSE data, AmirAli, any perspective you can share on the protein marker situation there? Was it a choice of marker? Or was it perhaps more related to adding those markers that's changed the way the classifier sort of [weighted] the non-proteomix markers that already there. Any insight on the performance degradation so far? Or is it still too early to tell?

Helmy Eltoukhy^ Great. Thanks, Tejas. Good question. So that's exactly the sort of balance we think about or the framework we think about as we launch new products,

essentially how much do we spend the sort of market share, to develop the market, take some market share versus how much do we wait until reimbursement comes in and given the competitive kind of environment we see, which is one where we are the only product that we know of that is tissue free.

And so that ultimately is the, I think, sort of product market that is required to take over the MRD market. We believe that we have the luxury to engineer demand where we can sort of move that pendulum and move that balance towards essentially reimbursed tests and really try to concentrate on that. And so that's why we're concentrating on CRC demand, I would say, for this term.

I guess the other thing I mentioned is that we're very excited in terms of the overall MRD market. I think it's moved very quickly. It's clearly going to be a major opportunity. But we see the tests out there just to give you another analogy like the [flip cam] back in like the 2000s were taught everyone how to use video cameras. Well, it ultimately didn't have (inaudible) smartphones came in and co-opted that functionality and improved on it. And we obviously talked about our smart liquid biopsy. We are that smartphone in MRD market.

AmirAli Talasaz^ And then maybe I take the CRC screening question. So in terms of proteomix they just -- still we are kind of learning from the data, already some learning has happened. For some competitive reasons, (inaudible) some of the -- our competitors maybe learn similar lessons themselves. But some of the interesting factors are like in these multiyear studies, samples coming from hundreds of sites different kind of shipment, temperature kind of oscillation samples go through, the kind of tubes that you use and so forth, there are many variables that could contribute in the performance or lack of performance of [INFINITY] biomarkers, including proteomics, but there are some learnings for us and we'll keep some of those learnings close to our chest at this time.

In terms of performance degradation, I'd like to know what we saw in terms of just this 83% CRC sensitive. On the one side, this is a small end study of like 65 CRC, so higher level of confidence intervals, 83% is actually 90%.

Having said that, we are really also learning some actually lessons and interesting observation that a fraction of some of these border line, early stage kind of CRCs, when the patients go through colonoscopy and that gets kind of removed, detecting of those cases with the tech stack and the training of algorithms that we developed have [lower] performance and the main reason from my perspective is in the case control early stage [asymptomatic] patients, those are the cases which are (inaudible) post colonoscopy. So that would explain some of this delta that we are seeing. But the good point is now we have bunch of these samples, a bunch of learnings from these samples. So there are potential path for us that over time, probably the performance can even get further improved from this 83%. So we'll see.

Operator^ The next question comes from the line of Derik De Bruin with Bank of America.

Derik De Bruin^ Could you go a little bit more into the biopharma market dynamics? There have been some other companies that have commented that they haven't really seen any impact from the IRA or this -- I mean we were on some of the CRO calls that we've been on have suggested that. So can you just talk a little bit more about the dynamics there? And I guess, is there also any competitive dynamic going on here from a -- the fact there's a lot of companies now that are now offering similar liquid biopsy products or competing liquid biopsy products. Just a little bit more on what you're seeing from a volume versus competitive standpoint? Then I have a follow-up.

Helmy Eltoukhy^ Okay. Yes, I can take that. I would say that where we're seeing, I think, some potential sort of headwinds with respect to IRA and frankly, just we work with over 150 biopharma companies and biotech companies and a lot of them are obviously trading below enterprise value and it's a difficult kind of macro conditions. A lot of the testing we do aren't necessarily the bread-and-butter trials, maybe the CROs are doing. We're doing a lot of retrospective analysis, research, research for follow-on targets.

I mean, obviously, a good part of our business is the bread and butter and the patient selection type business. And so -- we're seeing a whole mix of things. We're seeing some clients who were doing a lot more and others where they're sort of a (inaudible) do they delayed for 1 quarter and so on.

That being said, our pipeline is very strong. We came into -- with a very strong order book into '23. And so we're hopeful that some of these headwinds hopefully don't materialize. But obviously, we want to be kind of prudent in terms of how we look at the upcoming year. There's a second question.

Derik De Bruin^ Yes. Yes. Just have you had a presubmission meeting with the FDA? And if so, what's been the feedback on the trial, having run the 2 different variable assays, 1 with proteomics and without.

AmirAli Talasaz^ There are two different configuration devices on screening sites. So the -- as we mentioned before, we started with cell-free DNA only configuration, and then we added the proteomics. So we had that configuration of cell-free DNA only device, which was kind of in frozen in terms of device parameters managers, clinical threshold, everything before any clinical data base was actually got unblinded. So -- we believe we're not in a proper way in terms of the clinical planning, statistical planning and doing this in a proper way.

In terms of coordination with FDA, again, post COVID launch of these kind of pre-sub meetings and conversation with the FDA has been deprioritized and within the time line that we have it was not possible to do a pre-sub, go to a multi-month kind of a discussion to have realignment plan in terms of this kind of multi-device configuration testing. Having said that, we've done such kind of multi-configuration testing on our CDx before

and some other manufacturers have done it in other kind of IVD studies. But we'll see when we go through FDA review. We believe we have that in a proper way.

Operator^ The next question comes from the line of Jack Meehan with Nephron.

Jack Meehan^ AmirAli, I wanted to continue on screening. First, any thoughts on expected time line to publish ECLIPSE in a leading medical journal. And then kind of second, continuing on the FDA process. Just after the submission this quarter, what do you think the time line is for potential approval? And do you think they could commission a panel?

AmirAli Talasaz^ Yes. So in terms of the FDA process like we're planning -- this PMA submission is imminent now, like before end of this quarter, it's going to go out to the agency. In terms of review time line, we are going to have a better understanding of it after we get some initial feedback from FDA, which specifically have times like 100 days after submission. Based on our judgment before those kind of feedback from FDA, we expect that early 2024 would be a time line which is appropriate for our FDA approval.

But once we go through that kind of a (inaudible), we are going to have a better understanding. In terms of panel conversation, definitely, it's FDA's decision if they want to make that (inaudible). They've done that for Cologuard, they've done that for Epi proColon. But both of those devices were first of its kind for them to review and some up and downs we put devices during the review cycle. So now they are more experienced, but again, it's their choice if they want to call for a panel discussion or not.

Jack Meehan^ And on the medical journal?

AmirAli Talasaz^ Medical journal. So some aspects of publication time line is an external factor of like how long the review would take. But based on our internal kind of activities and having a paper ready for submission. We continue to expect to have the publication in a good peer review journal throughout 2023.

Jack Meehan^ Awesome. If I can ask 1 more follow-up for Helmy. This UnitedHealth decision would be great to get your thoughts. What do you think this means competitively for G360 CDx? And just financially, what could this mean?

Helmy Eltoukhy^ Maybe Mike talk about the financial side of it. But in terms of competitively, they only gave coverage to test with companion diagnostic approvals. And as you know, that's an extremely high bar. There are very few even tissue [NGS] tests in the space that has approval of PMA or FDA approval. It's not easy to get and easy to submit, but that's very hard on the CDx side to go through the entire process. And that is one of the many moats we have in our business.

And I think Dirik talked about competitive pressure. We're not seeing any of that on the pharma side. And even on the clinical side, as we said in the prepared remarks, we are seeing -- maintaining is not expanding our market share despite the number of newer

entrants and if there's 35 entrants or 37 entrants, it frankly hasn't mattered over the last 8 years. Some of them had billions of dollars to spend yet could not crack essentially the market that G360 continues to command in therapy selection.

Mike Bell^ Yes. Maybe I can add from a financial perspective. it's positive news with United. We don't have any [increase] backed into our assumptions in 2023 and our guide for this. And Guardant360 ASP, our assumptions still it's going to stay in the same 2,600 to 2,700 range. And because of the way we recognize revenue and the timing of getting payments from payer, it is going to take a bit of time to start to -- if we can see the impact. But maybe to quantify if we were to get a \$100 increase in our ASP on Guardant360 that's over a \$10 million increase to our revenue. So we're looking that closely, and we're seeing traction potentially with other payers. So there's room for upside, but it's not baked into our numbers at the moment.

Operator^ The next question is from the line of Julia Quin with JPMorgan.

Ruizhi Qin^ So first off, just following up on the G360 breast -- it's taken many years for lung cancer to reach 15% penetration today. What do you expect the best penetration curve to look like compared to [lung] whether in terms of patient or payer mix? And are there any lessons that you've learned from your lung experience to drive a potentially faster adoption in breast longer term?

And then my second question is for my -- regarding the new U-Screen study on compliance, can you help us understand how important this is to support guideline inclusion, what kind of goalposts do you hope to achieve in a real-world setting versus that 90% compliance that you've currently seen in your early launch experience. And given that the scope of the study only includes noncompliant population, will be limit the scope of guideline inclusion for Shield?

Helmy Eltoukhy^ In terms of the breast cancer approval, that is what drives adoption is essentially the therapeutic options for patients and really making the fact that testing needs to be top of mind in order to access those life-saving options for advanced cancer patients. And so traditionally, breast cancer hasn't had many kind of therapeutic options. Lung is sort of in the canary in the coal mine, but we're starting to see breast cancer with PIK3CA mutations, now ESR1 and a host of others, really require the need for genomic testing upfront. But what's unique about this approval, though, is the fact that this is often an emergent [resistance] mutation. So it's often not kind of inherent to the primary tumor.

And that means that the only way to really assess that in a feasible manner is through blood. And we are the only companion diagnostic for this new class of therapy, the ESR1 type mutation-driven therapies. And so it's very exciting. It's why it's a big opportunity. We're already seeing really nice kind of volume increases because of this approval. And we're hopeful that paves a way for as you've said, faster adoption in additional cancer types, including breast cancer.

AmirAli Talasaz^ And regarding the U-Screen and actually the studies that we are doing to show the improved adherence to colorectal cancer screen using blood test. So U-Screen would be a piece of the puzzle in terms of -- it's 1 of the prospective studies that we are doing, which, in combination with a series of all other evidence that Guardant is going to generate and some other health systems and partners are going to generate would really not only pave the path for guideline inclusion, but also for commercial adoption of such tests over time.

I expect that as we talked about, we have this real-world evidence, more than 90% adherence rate. And I expect before USPSTF guideline inclusion guidelines get updated, we are going to have a series of these kind of data coming to the field. U-Screen is first of a kind in a sense that it's a prospective study that we are supporting. In terms of the impact of this and the fact that we are just testing the patients who are noncompliant at this time, those are the patient population, which are the hardest one.

So imagine that if we show very high actual compliance in those patients, we are talking about some of the pockets of the health system that the current compliance rate is between 40% to 50% even and showing a good fraction of those patients are, in fact, when they get access to blood test, they're kind of conflict of blood tests, which generate a huge value for us that even those patients are compliant.

Operator^ The next question comes from the line of Puneet Souda with SVB Securities.

Puneet Souda^ So first one on Reveal. I mean I appreciate the growth of 250% here. But as we -- as you look at the data, the trials here, Pegasys, Cosmos, TRACC, the most of the readouts are in 2024. So should we be thinking about reimbursement for REVEAL in 2024 mostly for these indications? And then on Smart Liquid Biopsy, how do you incorporate that into REVEAL? Do you have to generate new data? Or how do you insert that into these ongoing trials?

Helmy Eltoukhy^ Yes, great question. So these are just highlights of some of the, I would say, more pivotal trials. These are pivotal in the sense that they're largely interventional. So these are sort of data sets that really haven't really been seen in this kind of prospective fashion in the field in terms of really establishing clinical utilities, especially for the private payers. In terms of thinking about Medicare reimbursement, we have many other data sets around clinical validity that are not highlighted here that and hopefully, some of them will be able to be published or presented this year I don't know the second part.

Yes. So that's reveal transition. So yes, that's something that obviously has been in the works for some time. And so many of these studies either have kind of bridging points or are essentially going to be carried out using the sort of new version of Reveal in the Smart liquid biopsy. That sometimes it has been mapped out, and we're confident we can make a very graceful transition.

Puneet Souda^ Got it. And then if I could ask on the screening side. I mean, just given the focus on cash burn and cost reduction here, can you just outline what your priorities on potential indication expansion for Shield into other tumor types? And sort of how should we think about given the other competitors that are working on multi-cancer early detection. How should we think about your position there beyond CRC and the investments you have?

AmirAli Talasaz^ So CRC is our first indication, as we've mentioned before, actually, we are pursuing the lung cancer indication very seriously as well. So we are doing our registrational study, 10,000 patients screening study for high-risk patients who should go through lung cancer screening.

We are in the second year of enrollment, it should be probably around 3-year enrollment study. And as we mentioned actually in our prior presentation, we are expecting to get some kind of addition of visibility data in lung cancer study that actually we've done with SFA and UCSF since 2017. We expect that readout to be sometime later this year or early part of 2020.

Operator^ The next question is from the line of Matt Sykes with Goldman Sachs.

Matt Sykes^ Mike, maybe just 1 quick 1 for you. Just as you talk about the implementing efficiencies in workforce reduction, and the drop in OpEx in '23. Could you maybe talk about sort of R&D versus SG&A and where some of the big levers are particularly in the workforce reduction side, what you've done and kind of think about how we should kind of see that split over '23 as we move into '24.

Mike Bell^ Yes. I would say on the workforce reduction, it's pretty much across all areas of the business. So it's not really weighted in any specific areas. So we see a bit of that impact across each of the lines. I think moreover, on the OpEx side and how we sort of bring the run rate down and how we bring the overall full year below 2022, it's probably primarily focused on the R&D line. I'd say SG&A is going to be relatively flat year-over-year, especially on the oncology side, we're still continue to invest on the commercial side to really drive the opportunities that we have.

I think on the R&D side, for the first half of the year, we'll probably see a similar spend as in the latter half of last year. But then as a lot of the studies that we've been doing start to drop off, and we're going to be carrying on with ECLIPSE at least for the next few months, as we continue to build up the biobank. By the second half of 2023, we'll see the R&D expense start to significantly come down. And so that's how we look at our OpEx as well. I think (inaudible) really dropping off in the second half of the year.

Operator^ The next question comes from the line of Dan Leonard with Credit Suisse.

Dan Leonard^ Two questions. first off, on the sales guidance, it would be helpful if you could characterize what trends you've tried to bake into your outlook versus what you've left as potential upside? And then for my follow-up question, Helmy, I want to make sure

I understand your answer to Puneet's question on the Reveal upgrade. Like how do those logistics work for trials that are already in flight if there's an interventional trial and a physician has made a therapeutic decision, how do you change the assay? I'd just like to understand that.

Mike Bell^ I think I am going to start off on the trends. Yes, I think there's a few trends that we've definitely baked into that. I mean, while we mentioned the clinical volume. And the real revenue driver in there is Garden 360. And so we continue to make in strong consistent growth year-over-year with Guardant360. So and that's the real revenue driver in that I just mentioned from the ASP point of view, with Guardant360, we're assuming that stays constant to last year, 2,600 to 2,700 range. But with commercial payers sort of coming on board, I think there's opportunity maybe in the latter half of the year for the ASP to start to improve.

I think there's other things that could also drive an upside, and that would be reimbursement in Japan. We're expecting that some point in this year and Guardant Response, we still have reimbursement for that. That was to come. That will be a positive for us. And then I think we've talked as well about a we saw 25% year-over-year growth in just the last quarter. We've mentioned low double-digit growth on the biopharma side. So we're baking that into our revenue guide, obviously, because we want to be conservative about the spend of the biopharma customers. So there's, again, a potential for that to improve over our expectations.

We continue to see a similar growth rate as we did in the last quarter, then obviously, that again would be an upside. And how we mentioned here, we see a good order book -- but I think we just want to be very conservative on how we're looking at the biopharma business. And then the development services, we've said that will be over \$50 million. That's, again, it's quite a lumpy line, a lot depends on the timing of -- with partnerships. And again, I think we were looking at that in a conservative way. And if things were to accelerate above what we're planning, and that could also book the trend upwards.

Helmy Eltoukhy^ Yes. In terms of the cutover, I mean, you're absolutely right. There already enrolled patients, and we race target enrollment, that's not a trial that we're going to cut over to the new platform, and the results will be from the old one. But for trials that are shown in the early innings, we haven't quite started. We obviously knew this transition was happening. So a number of those trials. We ensure that we're already testing with with Smart Liquid biopsy platform where we waited until it was ready to start those trials on those clinical validation data sets.

Operator^ Our last question today comes from the line of Patrick Donnelly with Citi.

Patrick Donnelly^ Maybe just another one on the profitable growth side. As you think about -- and it's following up on one of the earlier questions about that kind of the funnel on the screening side, how do you think about that piece? And then similarly, just on the international opportunity, Helmy, have you changed kind of the trajectory of some of the investments to build out, again, both the screening pipeline and then some of the other

opportunities there. And then just a quick follow-up for AmirAli, on the PMA submission. Just I know you guys were initially talking early 1Q. Just the confidence that it happens in 1Q and what has to happen to get it done.

Helmy Eltoukhy^ Just on international. It's an area that we think is a big growth driver for us, (inaudible). Obviously, the standard of care is that we're establishing with therapy selection, MRD and screening are going to save lives not just in the U.S., but globally, Japan and obviously, the first opportunity for us to establish a really big market outside of the U.S. We're really excited about our partnership with Adicon and the lab that is being set up in China to be able to access both biopharma and eventually patients there. And then obviously, in Europe, we have a number of labs there.

So we're taking, I would say, a very systematic and I think, disciplined approach to investment where we're doing the -- investing in the activities that will get us as quickly as possible to public reimbursement or I think gross margin positive kind of revenue in each one of those localities.

AmirAli Talasaz^ Regarding PMA time line, it's going to be Q1. So it's imminent. It's almost done. It's going to be done by this quarter.

Operator^ That concludes our Q&A session as well as the Guardant Health fourth quarter and full year 2022 financial results call. Thank you all for your participation.

You may now disconnect your lines.