Guardant Health ($55.40,GH)

- Guardant has two new liquid biopsy products that look to be ramping fast and are well positioned.
- Massive TAM to go after
- Shield could be the start of a very big thing for GH, and Q2 2025 showed very encouraging momentum.
- Shield could make the company: revenues could increase from $60m this year to $700m in 2028 with potential upside if Shield becomes a multi-cancer screening platform.
- We think Guardant has a meaningful first mover advantage.

Sept 17, 2025

Potential Upside: $150 (+170%) over 3 years
Sensible Downside: $23(-50%)

The cure for cancer is early detection

- **Guardant Health is a leading precision medicine company focused on "conquering" cancer with data.**
  - Guardant Health is a leader in liquid biopsy, a blood test, for cancer profiling.
  - For the basics, such as what is liquid biopsy, please see this 2020 report.

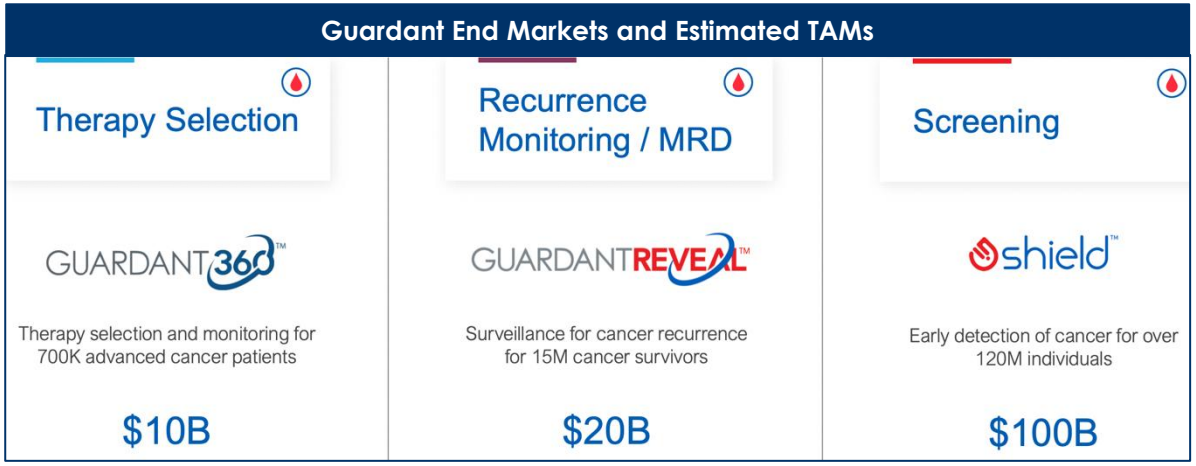
- **The therapeutic landscape for cancer has transformed significantly with the advent of precision oncology.**
  - Personalised medicine in cancer treatment means that it is critical to give patients the appropriate molecular therapies at the right time to improve clinical outcomes.
  - Traditional tissue biopsies, the current standard of care, are often not feasible for repeated use due to their invasive nature.
  - **Liquid biopsy has emerged as a pivotal modality due to procedural ease (a blood sample).**
  - **This capability is critical for precision oncology, as well as newer markets such as cancer screening.**

- **The science behind liquid biopsy is no longer a debate, however changing workflows in healthcare takes time.**
  - Modality matters: Taking blood is much easier than taking tissue and the test turn around times are much shorter.
  - **GH, and indeed all the competitors, are betting on the continued growth in liquid biopsy replacing traditional methods to get data on what is ailing a patient.**
    - E.g. NTRA: Panorama NIPT test is replacing amniocentesis to test for fetal abnormalities such as Down syndrome.
    - The tests use fragments of DNA that are found in blood, known as cell-free DNA (cfDNA).
- If humanity decides that they want to 'cure' cancer, increased early detection is critical, combined with gene targeting drugs. **This is the trend that Guardant, NTRA, GRAIL, EXAS play into.**

- **Guardant (GH) is a product cycle play, with two new liquid biopsy products on the market.**

The markets GH is going after:

- Three use cases:
  1. **Cancer early detection**: Screening for cancer markers in the blood
     - This has just been launched in CRC (Colorectal cancer)
  2. **Treatment decision making:** Companion diagnostics to select the best treatment.
     - 360 is the most mature Guardant product, FDA approval in 2020.
  3. **Post-treatment monitoring / molecular residual disease (MRD) detection:** answering the "has the cancer come back?" question.



- **The opportunity is very large: >>$100bn vs Industry revenues of ~$3-5bn**
  - MRD and Screening markets are just starting. GH products have just hit the market.
  - Therapy selection: GH sees Lung, Colorectal, and Breast as ~30% penetrated in terms of CGP (Comprehensive Genomic Profiling),
  - **International expansion will approximately double the TAMs.**
    - E.g. Japan open to CRC products

The bet: product momentum

- **Guardant just raised 2025 revenue growth guidance**
  - Product growth coming from:
    1. **360 and Reveal:** reported in Oncology
    2. **Shield**: reported in Screening

Guardant raised 2025 Revenue Guidance

Revenue	Current Guidance	Prior Expectations
Total	**$915M – $925M** 24% - 25% y/y growth	$880M - $890M 19% - 20% y/y growth
Oncology	~20% y/y growth	~18% y/y growth
Biopharma & Data	Mid-teens growth	Low double-digit growth
Screening	**$55M - $60M** 68K - 73K Shield volume	$40M - $45M 52K - 58K Shield volume

Product momentum across each segment

- **We believe the TAM is real, and we are clearly very early in penetrating it. GH has the first blood based screening product hitting the market now.**
- **Shield could be the start of a very big thing for GH, and Q2 2025 showed very encouraging momentum.**

- GH is a very science first and patient-driven company.
  - **A key question right now is can they adapt to being a commercial /sales driven company?**

Model: Upside

- **Product / market success scenario:** The bet is mostly on product success / revenue growth. Particularly Shield.
- **Best expectations**
  - Shield volume/ASP comes in ahead; higher ASP and COGS improvement drives GM improvement
  - Oncology growth remains strong for the next few years due to Reveal (a new product) adoption

Guardant Health	2020	2021	2022	2023	2024	2025E	2026E	2027E	2028E	2028E
Revenue	**287**	**374**	**450**	**564**	**739**	**923**	**1,152**	**1,493**	**1,835**	**2,328**
Revenue Growth (YoY)	**33.8%**	**30.3%**	**20.3%**	**25.5%**	**31.0%**	**24.9%**	**24.8%**	**29.5%**	**22.9%**	**26.9%**
Consensus Revenues						922	1,120	1,370	1,740	
Segment Revenue										
Oncology	172	236	298	404	543	652	808	986	1,154	1,327
Biopharma & Data	65	68	94	136	177	205	226	248	273	292
Screening	-	-	-	-	5	58	110	250	400	700
Licensing & Other	50	69	57	24	14	8	8	8	8	9
Revenue Growth										
Oncology	70%	38%	26%	36%	34%	20%	24%	22%	17%	15%
Biopharma & Data	-19%	5%	38%	45%	30%	16%	10%	10%	10%	7%
Screening						1063%	90%	127%	60%	75%
Licensing & Other	49%	38%	-17%	-58%	-42%	-42%	-1%	2%	0%	12%
Gross Profit	**197**	**255**	**300**	**345**	**460**	**581**	**732**	**957**	**1,183**	**1,509**
GM	68.5%	68.2%	66.7%	61.2%	62.2%	62.9%	63.6%	64.1%	64.5%	64.8%

Shield: ~5years to get to $1bn in revenues.

Oncology has momentum for 2 years due to Reveal. Could be longer.

Product momentum

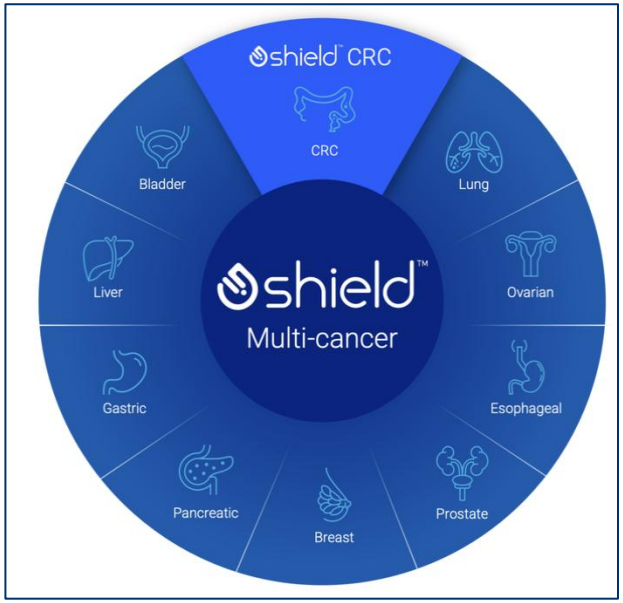
Shield: A cancer screening platform

- Survival rates are much higher when cancer is detected early:
- **Early screening and early diagnosis of cancer are extremely important because early metastatic cases are curable**, while late / stage IV cases are often incurable.
  - E.g. in Colorectal cancer (CRC): If the affected tissue is removed and cancer cells are eradicated, **the 5-year survival rate for patients with CRC stage 1 or 2 is estimated at 91% . For stage IV only 15% of patients survive 5 years.**
    - Yet, in the United States, only ~35% of patients are diagnosed at an early stage of CRC, even though there are more screening options and ~60% of eligible participants have been screened.
    - In France, the participation rate for CRC screening tests is ~30-35%. It varies across other European countries, but usually about 60-70% for the west and Nordics, much lower in the East.

- **Cancer screening via blood draws is a new market that is just getting started. There is and will be significant competition, the market winners are not yet certain, however Guardant currently has a first mover advantage.**

- **Guardant's screening platform is called Shied:**
  - It is a blood based ctDNA test.
  - **Today, there is only one test: CRC.**

- **Future Vision: Multi-Cancer Detection:**
  - While currently approved for CRC, Shield was built with the long-term vision to be a "multi-cancer detection" screen, meaning it could eventually screen for several types of cancer from the same blood sample.



Source: 10Q

Shield: What is it?

- The Shield test is for adults aged 45+ who are at average risk for colon cancer. **It makes colon cancer screening easier for people who might avoid the other tests modalities.**
  - Guardant Shield is a blood test. Instead of needing a colonoscopy (camera imaging) or stool test (e.g. Exact Science Cologuard), a healthcare provider takes a blood sample.
  - If the test finds signs of cancer, the doctor will recommend a colonoscopy to confirm.

- **Key Features and Benefits:**
  - **Ease of Use:** It's a blood test, which is seen as **more pleasant and convenient than stool tests or colonoscopies**, leading to higher rates of people completing their screening.
  - **FDA Approved: Shield is the first blood test to receive approval from FDA as a primary screening option** for colorectal cancer.
  - **Medicare Coverage:** It also meets the requirements for Medicare coverage, making it accessible.
- **Important Considerations:**
  - **Cancer Detection, not prevention:** Shield is good at detecting existing colorectal cancer (83% sensitivity), but it has limited ability to detect advanced adenomas (pre-cancerous growths).
    - For cancer prevention, which involves finding and removing these adenomas, colonoscopy remains the gold standard.
  - **Not a Replacement for Colonoscopy (for now):** For individuals who are willing and able to undergo a colonoscopy, especially if they are at high risk, colonoscopy is still the preferred option.

- **Accuracy**
  - Shield demonstrated **high detection of Stages II, III, and IV**, with a 81.5% sensitivity to Stage I-III colorectal cancer. (link)
  - Based on data from clinical studies, Shield has limited detection (55%-65%) of Stage I colorectal cancer and does not detect 87% of adenomas (precancerous growths).
  - **Note that one of the push backs is that Shield has lower accuracy than the EXAS CRC test, which is now 95% sensitivity for the Cologuard plus test.**

Shield's value proposition

- **The lack of compliance for stool-based tests is the main demand driver:**
  - Existing stool-based screening methodologies have been around for a decade or more, yet there has not been a material change in screening compliance over the last several years.
  - There are ~50 million U.S eligible patients who remain unscreened, and for those that have been screened, their re-screening rate has been poor.
  - **The crux of the problem being that those 50m patients need a new modality if they are ever going to be screened.**
    - Unscreened individuals who were surveyed had a strong preference, five-to-one, for blood over stool. (not really a surprise)
    - In one survey ~70% of individuals who have been previously screened for CRC with a stool-based test said they would not choose to screen with stool again.
      - Note that prescribing doctors have a very strong preference for colorectal exams and stool based tests today.
      - The challenge is that the patient experience is 'less than ideal.'

- **The ease of use of a blood test and the ability to screen patients during routine care is the main driver for Shield.**
  - Blood testing is already entrenched into routine patient care - 87% of people aged 50 and above have seen their doctor during last 12 months, and 91% of that group has had a blood draw in the last 12 months.
- **Early detection saves lives & is cheaper**
  - **Colon cancer** is the **second leading cause of cancer death** in the U.S.
  - Caught early, survival is very high (~91%).
  - Late detection costs healthcare systems hundreds of thousands of dollars per patient. Early detection thus has a large clinical and economic value.
- **Shield is the first FDA-approved blood test for colorectal cancer screening.**
  - Meets Medicare coverage requirements (≥74% sensitivity, ≥90% specificity).
  - Already included in **NCCN guidelines** (June 2025). This ensures doctors see it as a mainstream option.
- **Promising platform for multi-cancer expansion**
  - The same technology is evolving into Shield MCD (multi-cancer detection). If proven, Shield could move from CRC screening to a universal blood test for many cancers, which would be a transformational opportunity in healthcare.

Q2'2025 showing momentum as Shield ramps-up

- **Strong revenue growth and 2025 guidance:**
  - Guardant raised its full-year 2025 Shield revenue guidance **to $55 million to $60 million (from $40 million to $45 million),**
  - Expected test volumes of **68,000 to 73,000** (from 52,000 to 58,000)
  - **Shield's gross margin increased significantly** to 48% (from 18% in Q1 2025 and 2% in Q4 2024).
    - ASP was >$900. The cost per test reduced to <$500.

Guardant ($M)	2018	2019	2020	2021	2022	2023	2024	Q1 25	Q2 25	Q3 25E	Q4 25E	2025E	2026E
Revenue	91	214	287	374	450	564	739	203	232	236	251	923	1,126
YoY Revenue growth			33.8%	30.3%	20.3%	25.5%	31.0%	20.8%	30.9%	23.3%	24.4%	24.9%	22.0%
Segment Revenue													
Oncology	44	101	172	236	298	404	543					652	782
Biopharma & Data	35	80	65	68	94	136	177					205	226
Screening	**-**	**-**	**-**	**-**	**-**	**-**	**5**	**5.7**	**14.8**	**17.0**	**20.0**	**58**	**110**
Licensing & Other	12	34	50	69	57	24	14					8	8

- **As previously stated, Shield growth is dependent on GH ramping its sales reps and market demand**
  - Sales-rep take ~6-12 months to become fully productive
  - **By year-end 2025, Guardant expects to surpass 250 sales representatives, with a long-term goal of 600-700 reps for nationwide coverage.**

- **Market demand point of debate:**
  - Will the blood modality be the critical factor? Or will headline accuracy?
  - **Our opinion is that the blood modality will be much more important.** 50m people have not screened because they don't like the current options.
    - Thus doctors will probably accept the lower accuracy, as long as the testing happens especially for low risk patients.

How big can Shield become? Very big!

- **Guardant believes they can get to 1m in shield test volume in 2028**
  - $500 per test
  - 1m tests at $500 is the basis for GH's target of $500m in revenue from Shield.
  - **GH believes that the COGS would be ~$200 at that scale, i.e. a 60% GM business.**

- **Commercial opportunity: The "first-line" screening population (~65 million)**
  - Guardant (and indeed all the competitors) estimate that ~65 million Americans fall into the currently eligible, average-risk, first-line screening group.
  - "First-line" here means people due for screening, not those being followed up after polyps, symptoms, or past cancer.
  - These are the people choosing between colonoscopy, stool tests, or now, a blood test.
- **The screening gap (~50 million are not up to date)**
  - Out of that ~65 million about 15 million are up to date with screening (colonoscopy or stool).
  - But **~50 million have never screened or are not up to date.** They should get screened based on guidelines, but they are 'choosing' not to, even though colonoscopy and stool-based tests have been in the market for some time now.
  - ~135m Americans are aged between 45 and 85.
- **Potential upside could be large: a 15m annual testing opportunity?**
  - Recommendation is that patients using Shield are retested every three years. (The same frequency as Cologuard)
  - **At $500/test = $7.5b TAM for the 50 million unscreened people in CRC.**
  - Guardant thinks it could have 60% of this addressable market. Clearly highly speculative right now with several players emerging.
- **International opportunity:**
  - Building on the US approval, **GH is pursuing clearance in Europe, Canada, Australia, and select APAC regions**.
    - Canada: Guardant teamed up with Bayshore HealthCare, a major provider of home and community healthcare, to offer Shield
    - **In January 2025, Abu Dhabi selected the Shield test as part of its blood-based colorectal cancer (CRC) screening initiative. The pilot is targeting ~10,000 individuals for screening in its first year.**
    - GH is investing to accelerate Shield's global commercial infrastructure, including direct sales teams and support services in major international markets.

Shield's next step
Multi-cancer screening platform?

- **Multi cancer screening is very early**, however given the potential, and the probable ability for blood based tests to be multi-cancer, GH looks to have a strong first mover advantage in what will be a large market at some point.

- **GH's vision has been for Shield to evolve into a multi-cancer screening platform, capable of detecting various cancers from a simple blood test during annual check-ups.**
  - This is no different from the rest of the industry. It seems clear that this is where the industry is headed.
  - Shield was granted Breakthrough Device Designation by the FDA for multi-cancer detection in Q2 2025.

- **National Cancer Institute's Vanguard Study**
  - In January 2025, Shield was selected for inclusion in the National Cancer Institute's (NCI) **Vanguard Study, a 24,000-patient pilot study evaluating multi-cancer detection (MCD) tests.**
  - **Shield was one of only two technologies selected**.
  - The initiation of this study establishes the clinical and operational readiness of Shield MCD.
  - GH is looking to broadening access to Shield MCD beyond the scope of the Vanguard Study in the near future.
  - **The NCI Vanguard Study commenced in early Q2 2025**

- **Shield MCD validation (Q1'25)**
  - Validation performance data for Shield MCD was presented at AACR, showing:
  - **Sensitivity in six aggressive cancers** (esophageal, lung, liver, pancreatic, ovarian, gastric) was 74%, **ranging from 67% (lung) to 96% (esophageal and gastric)**
    - **Overall sensitivity for 10 cancers of 60% (35% in Stage I/II, 84% in Stage III/IV) at a specificity of 98.5%.**
    - **Cancer Site of Origin (CSO) accuracy was 89%.**

Competition expanding from their core business

- **The market will be competitive, however GH has a first mover advantage**

- **Natera and Exact Sciences (EXAS) are both expanding into screening.**
  - Certainly assumed barriers to entry, such as data, do not seem to be having any impact on competition.
  - **Companies are leveraging strength in one area and expanding out into the newer markets.**
  - The colorectal space is the most competttitve, partly because it is the biggest market.

- E.g. Natera: **Natera aims to develop a blood-based colorectal cancer (CRC) screening test** using cfDNA
  - Natera has the Proceed Trial for early cancer detection. Currently enrolled ~3,500 patients from a target of 10,000.
  - Next readout from the study in the second half of 2025.

- E.g. **Exact Sciences (EXAS): Cancerguard screen for multiple types of cancers:**
  - **EXAS's own blood test failed to meet sufficient endpoints to be commercialy sucessful, so EXAS pivoted and did a deal with Freenome.**
  - **Freenome's Blood-Based CRC Test: called SimpleScreen,** detects ctDNA with 81.1% sensitivity for CRC (63.5% for Stage I) and 13.7% for advanced precancerous lesions at 90.4% specificity, based on the PREEMPT CRC study.
    - Exact Sciences acquired exclusive U.S. commercial rights to Freenome's current and future versions of this blood-based test for CRC screening, announced on August 6, 2025.

- **GH has an ~2-2.5 year lead over Natera and EXAS in blood based CRC screening** assuming that the current technology and results from the competition holds and EXAS,NTRA etc are able to reach approval.
  - NTRA and EXAS are particularly relevant because of the sales infrastructure they have built up already.
  - There are also other competitors such as GRAIL, Quest (DGX) and other private companies.
- **Will a blood test be the answer? Probably, at least in the near term: it will capture at least some of the 50m CRC market.**
  - How much? This will depend on GH's ability to ramp its commercial team, combined with market demand.

SHIELD TIMELINE:

- **We found this summary of how Shield came to market to be helpful**
  - **2015:** Guardant began working on liquid biopsy technology specifically for cancer screening
  - **2019:** Guardant began its large-scale ECLIPSE study. Enrolled 20,000 participants to evaluate the effectiveness of Shield in detecting colorectal cancer compared to colonoscopy.
    - **Dec 17, 2021: ECLIPSE study reached target enrolment.**
  - **May 2022:** Shield was launched and available as a **lab-developed test (LDT).**]
  - **Late 2023:** At Guardant's Investor Day, the company set a long-term target of 1 million annual Shield tests by 2028, with an implied revenue of $500 million and an ASP of $500
  - **Early 2024:**
    - Shield received a **positive recommendation from an Advisory Committee** for first-line CRC screening, following a 16-month review process.
    - Data from **ECLIPSE study was published** showing Shield outperformed guideline-recommended stool-based tests (FIT and multi-target stool DNA) in life years gained, CRC cases averted and prevention of CRC deaths.
      - Market disappointed that the sensitivity of Shield in CRC was not higher.
    - **Summary of ECLIPSE data: 65% sensitivity in pathology-confirmed Stage I, 100% in Stage II, 100% in Stage III, 100% in Stage IV; 88% sensitivity for combined Stages I–III.**
      - Noted: >20,000 real-world uses since 2022 with >90% completion after test-order.
  - **August 2024,** the **FDA approved the Shield blood test for colorectal cancer screening** in adults 45 years and older.
    - The first blood test approved by the FDA as a primary screening option for CRC and meeting Medicare coverage requirements.
    - Post-FDA approval, Shield demonstrated **83% sensitivity and 90% specificity in detecting CRC.** It also had **13% sensitivity** for advanced adenomas, a limitation Guardant proactively included in its proposed label.
  - **Q3 2024**, Shield received a Medicare price of **$920**, recognising it as an important new class of first-line CRC screening.
  - **Jan 2025 (effective from Jan 1):** CMS finalised a policy to remove cost-sharing for follow-on colonoscopies after blood-based screening tests for Medicare beneficiaries.
    - This ruling removed barriers to blood-based CRC screening and acknowledged the unique benefits to promote access to cancer prevention and early detection.
  - **May 2025: NCCN**, (guideline committee in oncology). Updated its CRC screening guidelines to include Shield in **Category 2A**, the same as other first-line screening modalities.

Oncology segment

Oncology segment

- Oncology is also seeing higher than expected growth:
- **Oncology, the largest revenue segment at GH is made up of:**
  - 360
  - Reveal

Guardant ($M)	2018	2019	2020	2021	2022	2023	2024	2025E	2026E
Total Revenue	91	214	287	374	450	564	739	923	1,126
YoY Revenue growth			33.8%	30.3%	20.3%	25.5%	31.0%	24.9%	22.0%
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Oncology Growth YoY				**70%**	**38%**	**26%**	**36%**	**34%**	**20%**
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Screening	-	-	-	-	-	-	5	58	110
Licensing & Other	12	34	50	69	57	24	14	8	8

- **Oncology volume grew 30% in Q2 2025** (to approximately 64,000 tests)
  - *"with the majority of growth driven by Guardant360 liquid, closely followed by closely followed by a strong contribution from Reveal."* Mgmt comments

- **360 is a more mature market, as the GH 360 test was approved in 2020.**
  - Approved for: tumour mutation profiling, also known as comprehensive genomic profiling (CGP), in patients with any solid malignant cancerous tumour.
  - Also approved as a companion diagnostic in non-small cell lung cancer patients with (EGFR) alterations.
  - Companion diagnostics tests are FDA-approved to identify mutations to guide treatment: For example, G360 non-invasive detection of ESR1 mutations in breast cancer.

- **Reveal is a newer product:** Plays into the 'MRD' market. MRD is screening for people who have previously had cancer.
  - **There's a huge unmet need for MRD** (Minimal Residual Disease Detection and Recurrence Monitoring) to help guide people's cancer journey.
  - **15M cancer survivors were diagnosed in the last 5 years. Tissue availability significantly decreases over time.**
    - **Less than half of patients are accessible with tissue based approaches**
    - Guardant is the only Medicare-covered tissue-free MRD liquid biopsy that is FDA approved.

360 Volume growth drivers

- **Long term market growth drivers remain strong:**
  - **Cancer treatment has and continues to see a significant shift towards precision oncology**, which seeks to match patients to personalized, targeted therapies based on the specific molecular profile of their tumours.
    - EGFR, ALK, ROSI, BRAF, MET, RET, ERBB2 (HER2), NTRK etc. genes have medications on the market today.
    - Secondly because cancer is heterogeneous and its genes mutate over time, what works as a treatment today, may not work as a treatment tomorrow.
  - Thus, **volume growth from increased testing as personalised medicine takes share of oncology treatments.**
  - **Plus, liquid biopsy is taking share from solid tumour biopsy.**
    - Liquid enables assessment of a comprehensive panel of genomic targets from a single sample, and second, it obviates the need for repeat invasive tissue biopsies.
- **Hence, the complexity of treatment options are increasing as there are more biomarkers being used and therefore Comprehensive genomic profiling (CGP) is a likely winner, be it liquid or tissue sample based.**
  - This is the fundamental driver for Guardant 360 volume growth.
- **Recent acceleration in growth may / may not be sustainable:**
  - *"third quarter of accelerating growth with the G360. A lot of that was propelled by the new features we've added, the new platform we're on with smart liquid biopsy."*
  - GH recently made an upgrade to the Guardant360 liquid biopsy test.
    - **The new enhanced test evaluates biomarkers in 739 genes in total, vs ~70 in the previous version**.

- **Guardant also launched a tissue test in April 2025.**
- The theory being that oncologists are already ordering tissue tests and GH reps are calling on the oncologist, plus tissue remains ~70% of the market.
  - **Guardant360 Tissue test enables insights beyond what can typically be found. The test enables classification and subtyping of each individual tumour at a much higher resolution.**
  - *"since Guardant360 Tissue is built on the smart liquid biopsy platform, it requires 92% less tissue surface area for analysis than the industry norm."*
    - *"more than 50% of tumour tissue samples from patients failed to meet the surface area requirement – meaning those patients couldn't qualify for testing."*

Example of what is happening cancer market

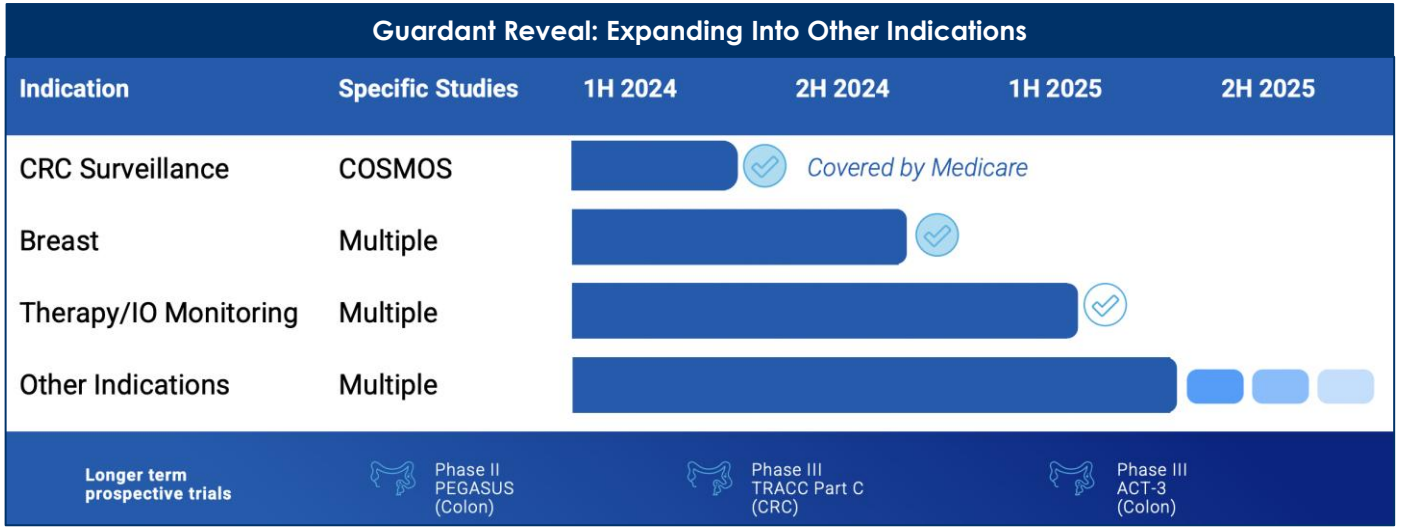
- E.g. **ORSERDU** (elacestrant), a selective estrogen receptor degrader (SERD) approved in January 2023 for ESR1-mutated, HR+/HER2- advanced breast cancer.
  - *Guardant360 blood test provides comprehensive genomic profiling to identify patients with ESR1 mutations who may benefit from ORSERDU targeted therapy*
  - In the clinical study, **people who took ORSERDU had a 45% reduction in the risk of their cancer growing**, spreading, or getting worse when compared to people who took other hormone therapies.
  - The median progression-free survival was 8.6 months on Orserdu, versus 1.9 months for standard of care

- **Several next-generation oral SERDs are in advanced clinical development**, many incorporating ctDNA-based monitoring for ESR1 mutations to guide intervention.
  - **Key Trial: SERENA-6 (Phase III)**:
    - Focuses on patients on first-line AI + CDK4/6 inhibitor therapy. Uses ctDNA monitoring to detect emergent ESR1 mutations.
    - **Results presented at ASCO 2025**: Switching to camizestrant **reduced the risk of disease progression or death by 56%.** was particularly effective in patients with ctDNA-detected ESR1 mutations, with benefits seen across subgroups.
    - **Emphasizes serial ctDNA testing for tumour evolution, enabling pre-emptive therapy switches**
    - If approved, camizestrant could become a standard for ESR1-mutated cases, further driving demand for liquid biopsies like Guardant360.
  - **Imlunestrant (Eli Lilly)**:
    - Data from ASCO 2025 showed imlunestrant significantly improved PFS in ESR1-mutated patients resistant to standard hormone therapy, outperforming fulvestrant (an injectable SERD).
    - Potential FDA submission in 2026.
  - **Vepdegestrant (Arvinas/Pfizer)**:
    - Key Trial: VERITAC-2 (Phase III)

- **We have no idea which drugs will be successful, but we do know that companion diagnostic tests will be required to select the treatment.**

Guardant Reveal: Breast is a new MRD indication

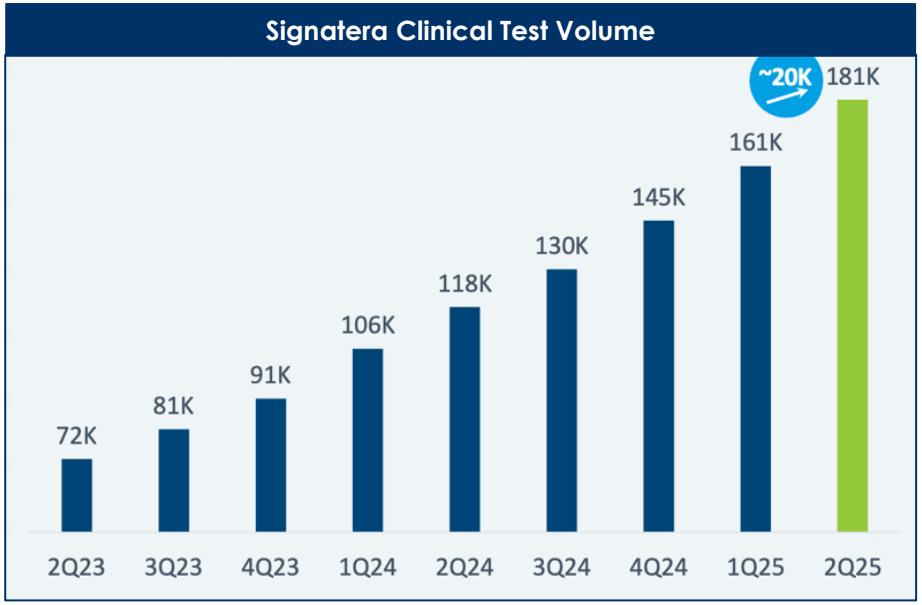
- MRD screening allows for earlier intervention than traditional imaging.
- Reveal started in colorectal cancer (CRC)
  - **Results demonstrated that ctDNA detected in the bloodstream after cancer surgery and prior to the start of adjuvant therapy is a strong predictor of the risk of disease recurrence**
  - 2,000 patients with stage III colon cancer with median follow-up of 6.1 years were presented at the 2025 ASCO meeting.
  - **Among patients with post-surgical ctDNA detected, 62.6% had the cancer return within 3 years, despite having had adjuvant chemotherapy, while only 15.4% of patients with undetectable ctDNA recurred in the same period.**
  - Validates the test as a decision support tool in the colorectal cancer setting.
- **Reveal has recently shown solid results in breast cancer:**
  - Guardant Reveal demonstrated **100% sensitivity for distant recurrence in patients with ER+/HER2- breast cancer** (about 70% of all breast cancers), and 71% overall, with 100% specificity and 100% positive predictive value for relapse.
  - We are at the point where Reveal has a compelling product, given that breast, CRC and IO, are the most significant indications in MRD.



Competition: NTRA's Signatera

- **Signatera is a ctDNA test for patients that have already been diagnosed with cancer. Owned by Natera (NTRA).**
- Signatera is a tumor-informed test for MRD. What does this mean?
  - **Signatera test requires both a tumor tissue and a blood sample. (whereas Reveal only uses blood)**
  - After Natera receives these samples, the test design and processing take 3-4 weeks to deliver the first result. This longer timeframe is due to the need to sequence the tumor tissue to create a personalized assay tailored to the patient's unique tumor mutations.
  - Subsequent tests are ~10days to get results.

- **Signatera is ramping volume fast:**

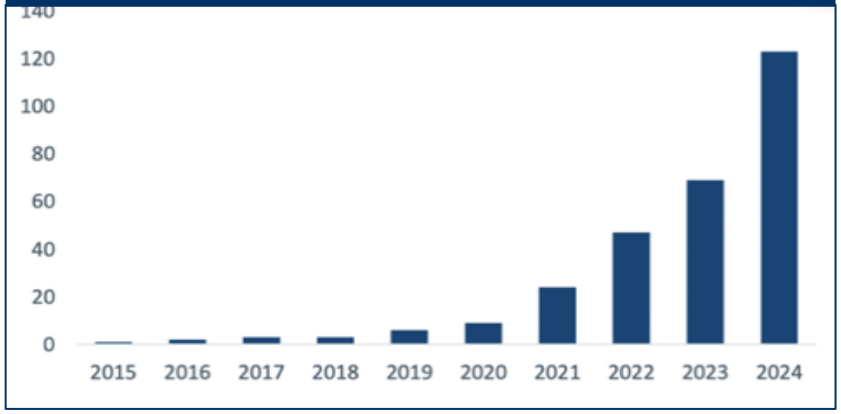


Signatera continued:

- **Cancers Covered by Signatera: All the big ones and the list is expanding.**
  - **E.g. Colorectal Cancer**: Used to detect MRD after surgery, guide adjuvant chemotherapy decisions, and monitor treatment response in metastatic cases.
    - Supported by studies like the GALAXY arm of CIRCULATE-Japan, showing high sensitivity for recurrence detection.
  - **E.g. Breast Cancer**: Used for MRD detection post-surgery, monitoring during neoadjuvant or adjuvant therapy, and identifying recurrence risk.
    - DARE Trial: Presented at ASCO 2025. The trial showed that 99% of patients without detectable ctDNA achieved relapse-free survival after a median follow-up of 27.4 months
    - More than half of patients who have breast cancer get some form of neoadjuvant care (to prepare the tumor or patient for better outcomes) before they go on to surgery.
  - **E.g. Non-Small Cell Lung Cancer (NSCLC)**: Supported by trials such as TRACERx and EMPOWER-Lung.

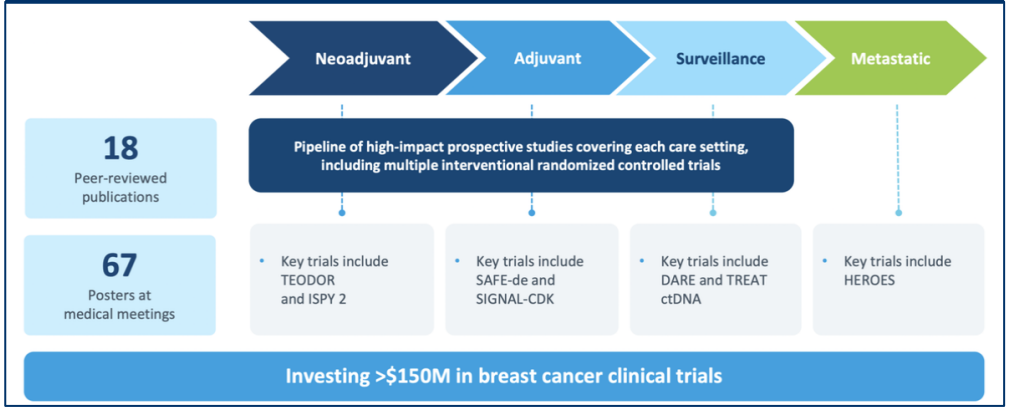
- **Note that Natera has said that they will continue to invest heavily in trials to expand the MRD usage.**

Signatera Cumulative Peer-Reviewed Oncology Publications



Source: Natera JPM conf presentation

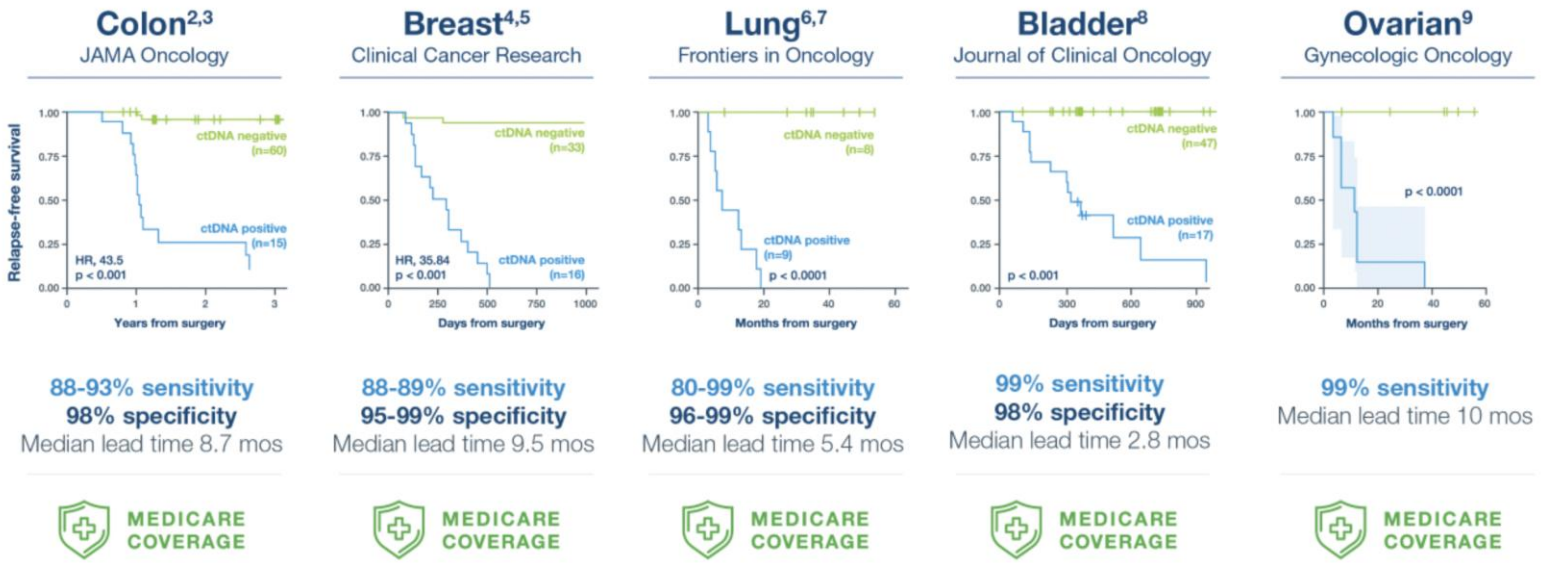
Signatera clinical pipeline in breast cancer



Signatera continued:

- Signatera is clearly ahead in MRD:

Signatera MRD Coverage



- **Guardant's Reveal will follow Signatera by expanding into other MRD indications.**
  - The big difference is that Signatera is tumor informed, which will not be possible for a portion of the market, perhaps up to 50%.

Reveal TAM and go to market

- **Estimated market TAM of 10m – 15m tests annually.** (US market)
- Reveal is differentiated in that it uses blood only, whereas Signatera uses a tissue-informed approach.
    - Does this matter? It might longer-term, but doesn't seem to right now.

- Guardant has published results for MRD in CRC and Breast cancer, just getting started in terms of volume ramp.
    - Leverages the G360 commercial infrastructure
    - Note that Reveal ASP is $600 to $700 vs total Oncology segment ASP of $2500.

- **So far Signatera seems to be winning the commercial battle**, however GH is very early in its ramp up.
    - Our take away has been that there is a commercial battle happening rather than a technology battle.
    - Singnatera seems to be winning in volumes, growing ~50% yoy and also in terms of commercial / sales execution.
        - NTRA comments suggest the longer term market will be a 'renewable' revenue type of market:
            - Split of test origination today: 50:50
                - 50% for adjuvant treatment (I.e. therapy given after the primary treatment (surgery) to reduce the risk of the cancer recurring or spreading.
                - 50% recurrence monitoring

- **Reveal is now at the point where commercial execution will be a critical factor in growing the business. GH needs to prove they can do it.**

ASP IS THE SECOND PART OF THE GROWTH

- **The ASP for Reveal will increase from ~$600 to $1,000 over the next few years.**
- **360 ASP improvements** :
  - Tissue: went from ~$1,700 per test to ~$2,000. (Q2 '25 comment)
    - "mid-quarter we upgraded tissue. We added the RNA element to the product.. that's reimbursed at the moment by Medicare at ~$300"
    - "***there's still quite a way to go with tissue ASPs***. *I think again Medicare advantage pull through and continue to work on the commercial pace, so we expect that to continue to improve over the near term.*"
  - In 2023 there was an increase in the Medicare rate for liquid 360, which increased from ~$3,100 to $3,500
    - *"and so we're starting to see now the pull-through with Medicare Advantage payers paying at a higher rate."*

- **Progress with commercial payers:**
  - **Commercial payers is a complex space, some pay, some don't reimburse the tests. For GH to get coverage from all insurance companies is a long battle.**
  - Commercial insurers typically align coverage decisions with clinical guidelines from authoritative bodies such as the American Cancer Society.
  - All the testing companies have the same problem. E.g. Natera:
    - **ASPs for Signatera is currently ~$1100, but NTRA sees a path to $2,000**. Same problem as G360 interms of Medicare Advantage and commefcial payers.
    - For example in Reveal for breast cancer: *"no, we're not getting reimbursed for that at the moment. And so when we get Medicare reimbursement for that, it's going to have a significant impact for us"*
  - Note that Reveal received Medicare approval in early 2025 for CRC.

- Medicare represented approximately 39%, 43% and 45% of precision oncology revenue in 2024, 2023 and 2022, respectively.
  - I.e. GH is making progress with insurance coverage as Medicare share of revenue is falling.

ASP WILL GET SOLVED, SLOWLY

- **State biomarker laws:**
  - Legislation has been enacted by ~21 U.S. states that mandates coverage of biomarker testing.
    - States include: Arizona, California, Colorado, Georgia, Illinois, Kentucky, Louisiana, Maryland, Minnesota, New Jersey, New Mexico, New York, Oklahoma, Rhode Island, Texas.
  - **These states require insurance coverage when the test meets specific criteria, such as: FDA approval or clearance, association with an FDA-approved drug, inclusion in Medicare coverage or clinical practice guidelines.**
    - I.e. it is just a question of the insurance companies making it easy for patients and companies to get paid, because the tests should be covered.

- E.g. Signatera is covered by Medicare for specific indications (colorectal, breast, lung, ovarian cancers).
  - **Natera management has said that they are 'educating' commercial payers in those geographies to update their approval processes. It just takes a long time.**
    - *"The reason we don't get reimbursed all that frequently for those patients is kind of the same reason. There's administrative hurdles to be solved."* Natera management

COMPETITIVE LANDSCAPE

- **NTRA: Believes there is plenty of room for new entrants. *"Competition is a good thing at this stage"***
  - "the adoption of MRD will improve the health of the population and take costs out of the system, it'll end up being fine for us as well." NTRA management

- Quest Diagnostics (DGX) is also entering, although not for quite a long time.
  - Acquired Haystack Oncology in June 2023 for $300 million in cash + up to $150 in milestone payments.
  - **August 25, 2025, the FDA granted Breakthrough Device Designation to the Haystack MRD test** for identifying MRD-positive patients with stage II colorectal cancer who may benefit from adjuvant therapy.
  - **The test is tumor-informed** (Uses genetic data from a patient's tumor to create a customized assay that tracks specific mutations in the blood)

- According to Guardant many of the tumour-informed tests still take four to eight weeks to get the results vs about 1week for Guardant.
  - We are unconvinced that this matters as much as sensitivity.

Financials

Operating margins?

- **A problem with the sector, and indeed GH has been the cash burning nature of the businesses before it has reached scale.**
  - Partly to do with R&D costs, partly to do with ramping up the sales effort.
- **Scaling the business is a critical bet over the next 5 years.**
  - Long-term model is ~70% GMs, 20% operating margins longer term. (vs. 63% - 64% GM today)
  - Today, any efficiency gains are going back into the business: e.g.
    - Mgmt comments on any incremental gross profit: "*putting that [back into] the sales and marketing line means our cash burn on screening isn't going to increase, and we can stay within this $200 million [cash burn on screening] for the next couple of years.*"

- **Profitability at GH is a number of years away as new products require sales and marketing investment.**
- **Shield commercial infrastructure build: Target is to build to 700 reps at some point.**
  - As of Q2 2025: the average tenure of sales reps is less than 8 months.
    - Reps take 6 to 12 months to start to impact revenue growth
    - **Q2 comment: expect to surpass 250 sales reps by year-end 2025**
      - In Q1 2025: expected 200 reps by end of 2025.
      - **Shield was launched in August 2024** with 50 reps, increased it to 100 through 2024. The vast majority of the people we added in late 2024.
  - 700 reps seems reasonable as 1000 reps seems to be about the number needed to go after the opportunity in CRC.
  - E.g. Exact Science has ~1000 reps in CRC.

- **Competition is facing the same problem although a little ahead of GH:**
  - NTRA turning the corner on profitability, although it is ramping investments.
  - EXAS is profitable at the Adj. EBITDA level and EPS is ramping fast the next few years.
    - EXAS has a multi-year productivity plan and a 2027 ltarget of 15% compounded revenue growth and >20% adjusted EBITDA margins.

Cash burn needs to be watched, but OK for now

- Cash burn on the Reveal and Shield tests has been reduced:
  - **The two growth tests (Reveal and Shield) have inflected to gross margin positive in 2025.**
    - E.g. Reveal COGS were 50% lower in 2024 to ~$500/test

- **Volume and revenue ramp is happening faster than expected:**
  - Q1 25: $5 million increase in Shield revenue guidance is due to higher volume
  - Expect 52,000 to 58,000 tests versus prior guidance of 45,000 to 50,000 tests.
  - **Late 2025 and 2026 is when we will see how the sales team can execute:**
    - **Full year volume to be more back-end loaded due to the time required for recently hired sales reps to ramp productivity.**

- GH has been reactive at managing the balance sheet.
  - E.g. Retired $659M of November 2027 convertible notes at 9% discount to par.
  - Issued new $600M convertible notes due February 2031
    - 1.25% coupon, 35% conversion premium at a $62.22 conversion price
- **$629m in cash**

- **Sales execution / execution risk is the main concern**
  - GH known to be a research heavy enterprise, question is can they adapt to being a good sales organisation too? We will find out in 2025 / 2026.
  - Reviews on glasssdoor = not good!!

- Guardant is holding its 2025 Investor Day on September 24th.

Model: Upside

- **The bet is mostly on product success / revenue growth**. Particularly Shield.
- **Best expectations**
  - Shield volume/ASP comes in ahead; higher ASP and COGS improvement drives GM improvement
  - Shield progress (including ADLT pricing benefits, potential ACS guideline inclusion, and long-term optionality with MCD)

Guardant Health	2020	2021	2022	2023	2024	2025E	2026E	2027E	2028E	2029E
Revenue	287	374	450	564	739	923	1,152	1,493	1,835	2,328
	33.8%	30.3%	20.3%	25.5%	31.0%	24.9%	24.8%	29.5%	22.9%	26.9%
Consensus Revenues						922	1,120	1,370	1,740	
Segment Revenue										
Oncology	172	236	298	404	543	652	808	986	1,154	1,327
Biopharma & Data	65	68	94	136	177	205	226	248	273	292
Screening	-	-	-	-	5	58	110	250	400	700
Licensing & Other	50	69	57	24	14	8	8	8	8	9
Revenue Growth										
Oncology	70%	38%	26%	36%	34%	20%	24%	22%	17%	15%
Biopharma & Data	-19%	5%	38%	45%	30%	16%	10%	10%	10%	7%
Screening						1063%	90%	127%	60%	75%
Licensing & Other	49%	38%	-17%	-58%	-42%	-42%	-1%	2%	0%	12%
Gross Profit	**197**	**255**	**300**	**345**	**460**	**581**	**732**	**957**	**1,183**	**1,509**
GM	68.5%	68.2%	66.7%	61.2%	62.2%	62.9%	63.6%	64.1%	64.5%	64.8%
Incremental GM	73%	67%	59%	39%	66%	66%	66%	66%	66%	66%
Research & Development	131	244	342	330	296	296	302	317	333	349
% of sales	46%	65%	76%	58%	40%					
yoy increase	52%	86%	40%	-3%	-10%	0.0%	2.0%	5.0%	5.0%	5.0%
Selling & Marketing	97	176	274	270	328	410	492	591	620	651
% of sales	34%	47%	61%	48%	44%					
yoy increase	24%	81%	56%	-1%	21%	25.0%	20.0%	20.0%	5.0%	5.0%
General & Administrative	67	87	121	129	133	136	149	161	161	162
% of sales	23%	23%	27%	23%	18%					
yoy increase	9%	30%	39%	7%	3%	0.0%	2.0%	5.0%	5.0%	5.0%
Operating expenses	**295**	**507**	**737**	**729**	**757**	**842**	**943**	**1,069**	**1,114**	**1,163**
Adj Operating income	**(99)**	**(252)**	**(437)**	**(384)**	**(298)**	**(260)**	**(210)**	**(112)**	**69**	**346**
Depcn	**14**	**20**	**33**	**40**	**40**	**43**	**51**	**62**	**70**	**73**
Adj EBITDA	**(85)**	**(232)**	**(404)**	**(344)**	**(258)**	**(217)**	**(160)**	**(49)**	**139**	**419**

Shield: ~5years to get to $1bn in revenues.

Oncology has momentum for 2 years due to Reveal.

Incremental GM stays at 66%

Operating margins only turn positive 3-4 years out.
Also, these are just guesses, the company could invest more, or not.

Valuation

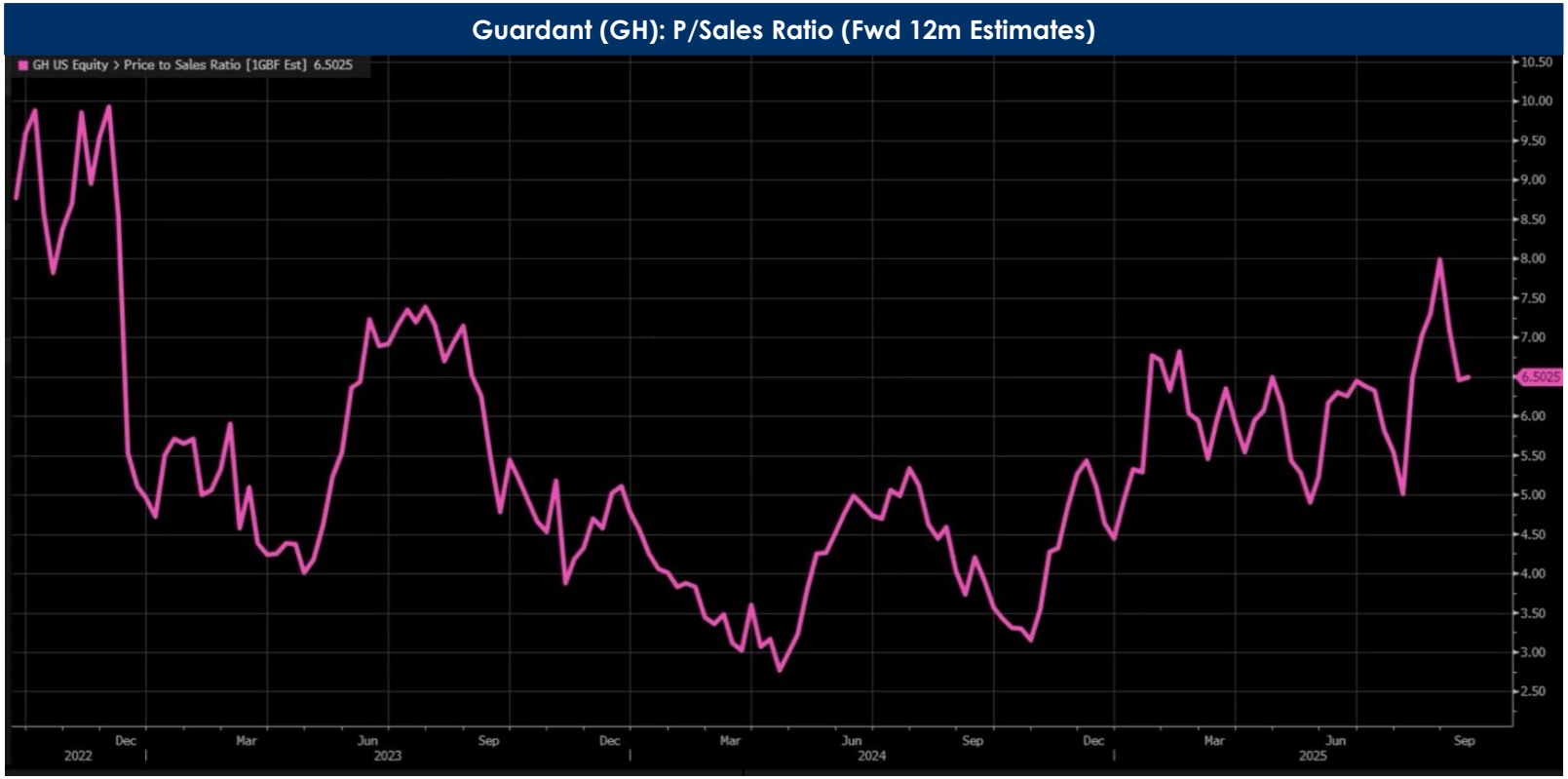
- **Valuation:**
  - **Price to sales is probably the best metric for the next few years, as GH needs to prove it can ramp up revenues, and then show that it can have high incremental operating margins.**
    - Near term it is all about proving the product is the right one for the market, hence revenue growth.
  - Peers:
  - NTRA in the 8-12x fwd 12month sales range.
    - The market has a high belief in its ability to compete with Signatera. We agree.
  - EXAS trades at about 3x fwd 12month sales
    - Concern is that EXAS is going ex-growth, or low growth given that the blood modality is arriving to CRC.
- **Growth:**
  - Oncology full-year 2025 guidance: "*expect total oncology volume to grow greater than 27% versus our prior expectation of greater than 25%.*"
  - Total **segment revenue growth is < volume growth as there is a mix shift towards Reveal,** where ASP is much lower.
  - **Oncology revenue growth guidance is for ~20% in 2025.**
  - 2026 should see a meaningful ramp in Reveal volume and ASPs.
  - On Shield growth, we assumed that it would be similar to EXAS speed of revenue ramp when they launched.

- **Upside: 10x $2bn in revenues** = $20bn, vs. 6.8bn mkt cap today and $7.5bn EV today.
  - No capital raises necessary, although we would not be surprised if GH raised some more equity in 2026/2027 to invest in growth.
  - **Hence >100% upside to $150 over 3-4 years. Based on >2bn in revenues in 4 years.**
  - Assumes 128m shares in 2028, vs 123m today, and that net debt increases by ~500m.

- **Downside:** to 3-4x revenues. Given the leadership in liquid biopsy, we think that if GH can't execute, someone else will.
  - **Gives downside to ~$4bn EV. Or a share price of ~$23.**

P/Sales range

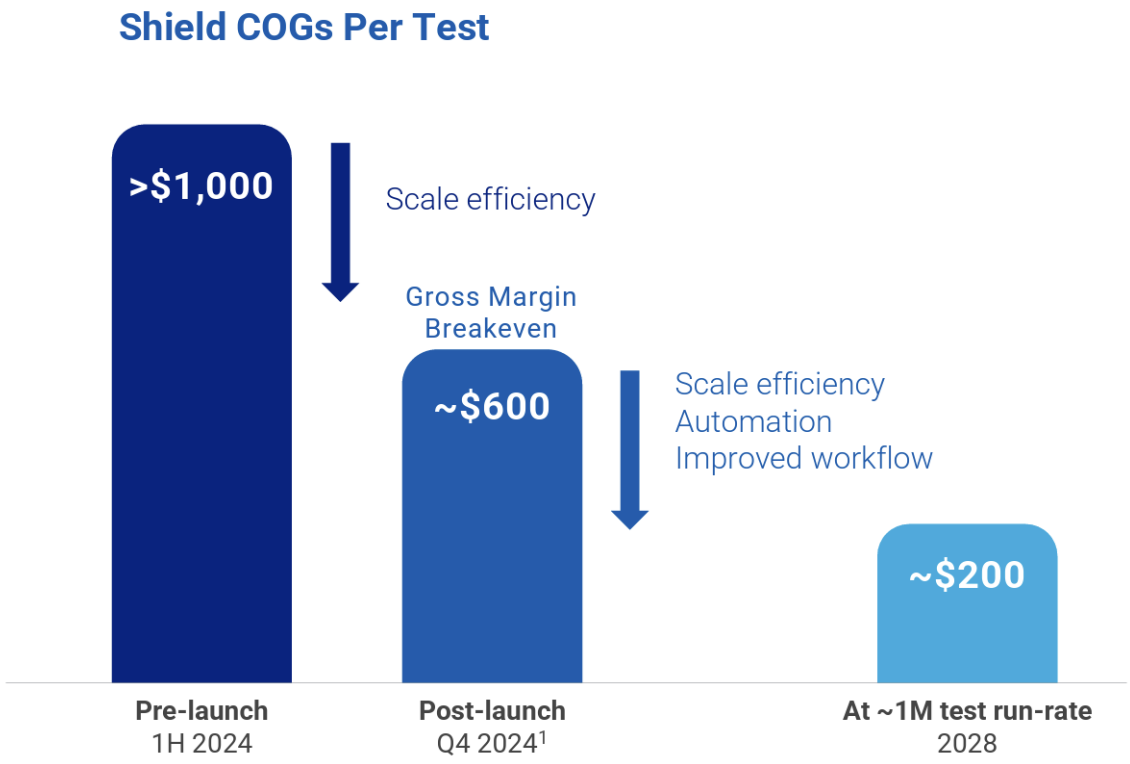
- GH: We think that GH will trade in the following range:
  - No faith in the platform/ technology: 3-4x fwd sales.
  - GH shows product growth and go to market execution, business will trade at 10x sales.



Appendix

COGS ECONOMIES OF SCALE

On track for **COGs reduction to ~$200**



GH – Jan 2025

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This research was produced by Vipin Ahuja, Partner and Robert Graham-Brown, Partner.