

# **Life Science Tools & Diagnostics**

# AGBT 2025 Takeaways – NIH Concerns and Genomics Competition in Focus

Coming out of AGBT, we have two big takeaways. First, NIH uncertainty is likely to have an impact of varying magnitude on Tools sales (in 1Q and likely beyond). We continue to see the most exposure on instrument sales into US academic customers. Second, is the high focus on competitive activity in sequencing. Roche is to be taken seriously as a new well-funded entrant, though it remains to be seen how the technology will translate from very early adopters to a full commercial launch. Focus companies include Roche, ILMN, BRKR, TXG, Ultima & Element.

#### NIH: Uncertainty Creating ST Capital Freeze

The uncertainty around the NIH was omnipresent at AGBT. It came up in almost every discussions with researchers and companies in Marco Island. One notable example was <a href="NHGRI">NHGRI</a> <a href="Director and AGBT committee member Eric Green">Director and AGBT committee member Eric Green</a> wasn't able to attend due to the travel ban.

We heard a lot of anxiety from labs proactively managing spend given uncertainty around indirect cuts. One researcher commented, "Everything has been slowed, it's not like a month ago." As researchers look at their budgets for the next 12-18 months, "We're definitely looking at capex." "This feels like an existential threat." There is also concern that grant review delays could have an impact on spending later in the year. The Trump administration had put a freeze on publication of grant reviews in the Federal Register. Some universities have started limiting hiring of post-docs. One researcher raised the question, "Who is going to run the instruments?" A final area of concern is around consolidation of NIH institutes. There has been discussion of potentially rolling up the National Human Genome Research Institute (NHGRI) into the National Institute of General Medical Sciences (NIGMS), which wouldn't be helpful for genomics industry.

Company feedback was mixed. We spoke with multiple private companies seeing an impact on demand for capital sales from US research customers to start the year. PacBio reiterated that they reflected some NIH pressure in their 2025 revenue guide, and that the impact of indirect cuts was "a real thing... it could extend sales cycles." In Illumina's analyst session, the company acknowledged customer concern. As one datapoint, CFO Dhingra stated half of 1Q shipments to date have gone to research (though this includes pharma & we need the denominator).

Customers are looking for alternative funding sources to diversify. One researcher described it as the "3 F's" (only one of which is an F) - Pharma, Philanthropy and Foundations. While uncertainty is freezing some purchasing activity, there is a partially offsetting dynamic that some researchers are pulling *forward* some work. If customers have budget to spend, some commented they want to take advantage of that before it becomes at risk.

What is it going to take for academic spending to get its mojo back? The industry needs a win. To start, researchers are searching for success stories to get in front of Congress to argue that they should support science. It's early to draw conclusions on the ROI from the NIH's All of Us program (which has sequenced 500K genomes to date). That said, there haven't been any notable breakthroughs (yet). If something were uncovered with clinical importance, that could be a catalyst for better spending (but visibility on that is low). A second win could be if there were increased scientific funding associated with generative Al. Large sample sets are needed to feed training algorithms. As a field, researchers are going to need to start showing utility.

Please see important disclosures at the end of this report.

#### **FEBRUARY 28, 2025**

# **Life Science Tools & Diagnostics**

Jack Meehan, CFA

646-214-0299 jack@nephronresearch.com

#### Tom DeBourcy, CFA

646-893-4706 tom@nephronresearch.com

# **Table of Contents**

| NIH: Uncertainty Creating ST Capital Freeze                            |      |  |
|--|------|--|
| Roche: Debate Is on the Path from Early Access to Commercial Launch    | 3    |  |
| llumina: Focus is on Multi-omics, Pipeline Seems Early                 | 7    |  |
| JK Biobank: Outlines Why Olink and Ultima Were Picked                  | 9    |  |
| Jltima Highlights Greater Throughput w/ Solaris, Progress in MRD w/ LH | . 10 |  |
| Element Bio: Innovation Roadmap Ahead of AGBT                          | . 12 |  |
| Bruker: Interesting Science, Tough End Market Exposure                 | . 14 |  |
| 10X Genomics and Other Single Cell/Spatial Tech                        | 15   |  |

## Roche: Debate Is on the Path from Early Access to Commercial Launch

The competitiveness of Roche's new sequencing launch was a recurring topic of discussion throughout the conference. The universal answer from the smartest people in the industry is that Roche needs to be taken seriously, but <u>MORE INFORMATION</u> is needed to make a call around how this will scale from early access to commercial launch. We heard bull arguments in favor of the system, we heard interesting critiques as well. It remains too early to speculate.

Here are the incremental thoughts that we have:

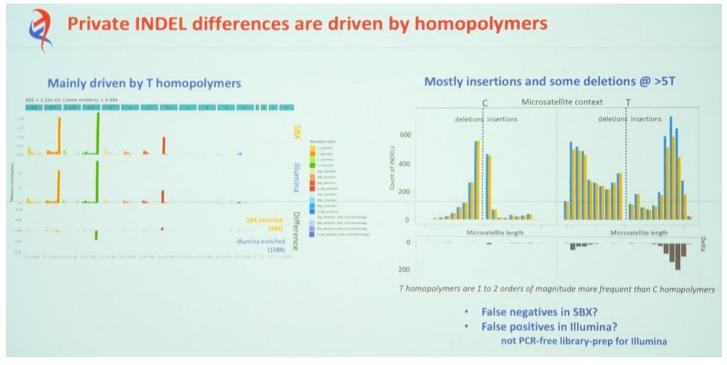
- Researchers and competitors are taking Roche very seriously. Roche has significant scale overall and in the Diagnostics industry, where they are the market leader. Unlike most of the current Illumina competitors (Thermo Fisher aside), Roche has an established business model, strong balance sheet and cash flow. Industry individuals were impressed with the amount of progress Roche made behind the scenes over the last decade to be in a position to unveil their system.
- Roche's <u>white paper is now available here</u>.
- Roche has been interacting with early access customers for about a year. These users only received the box within the last few months, and worked quickly to have data ready for AGBT. Early access customers were mostly pleased with the initial data generation. One highlighted to us that "It works," though there is still more to be done. From a workflow perspective, researchers highlighted the magnitude of the data generation, the speed of the system, and also less samples needed for a run. The mix of capabilities could make a compelling use case for rapid whole genomes in clinical settings. Research applications could include single cell analysis and PerturbSeq. It sounds like there is still some progress needed on the bioinformatics. The system uses GATK, and is also partnered with Google.
- Hartwig and the Broad Institute both presented data on Roche's system. Researchers commented that homopolymer data "looks really good, really solid." At Hartwig, the structural variation analysis is a "work in progress."

#### Fig. 1: Hartwig Summary Conclusions on Roche SBX

- SBX-duplex sequencing is suited for tumor-normal somatic variant calling
  - > Empirical platform SNV error rate for SBX is slightly lower than Illumina
  - > Small variant calls in patient samples are highly concordant
    - Most/all differences explained by stochastic effects involving real, low VAF subclonal variants
    - Source small number of private INDELS at homopolymers needs further investigation
  - Structural variant calling looks good but is work in progress
- Diagnostic performance would be highly similar to Illumina-based routine diagnostics
  - > No clinically relevant differences compared to Illumina-based routine diagnostics data in 30 patients
- > SBX provides a promising alternative platform for rapid WGS-based cancer diagnostics

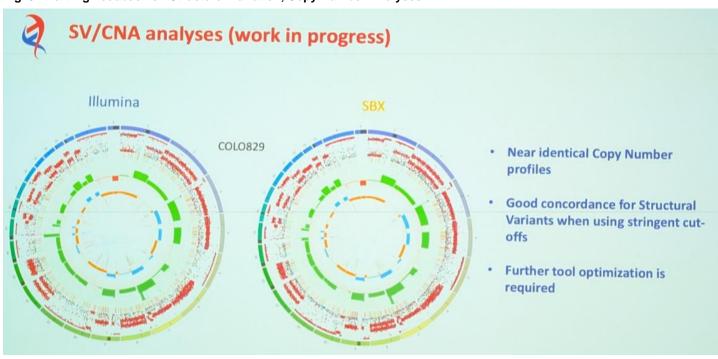
Source: Hartwig Medical, Nephron Research

Fig. 2: Hartwig Feedback on Insertion/Deletions and Homopolymers



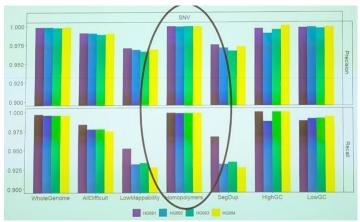
Source: Hartwig Medical, Nephron Research

Fig. 3: Hartwig Feedback on Structural Variation, Copy Number Analyses



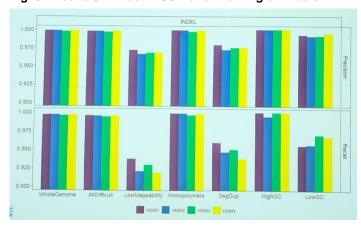
Source: Hartwig Medical, Nephron Research

Fig. 4: Roche SBX Fast WGS Benchmarking on SNVs



Source: Broad Clinical Labs, Nephron Research

Fig. 5: Roche SBX Fast WGS Benchmarking on Indels



Source: Broad Clinical Labs, Nephron Research

- On pricing, Roche gave a more forceful non-answer on pricing during their Silver sponsorship session. "We know what the market expectations are for high-throughput. This technology can meet all of those expectations for consumables and run costs. There will be different configurations for the box. We also know, in that price range, for mid and high-throughput, we are going to find different configurations in that range." More details will be shared in the future. So what does comparable mean? Customers are in the dark at the moment around the exact commercial strategy and what things that Roche will charge for to run the system. One researcher commented that "If Roche is at \$0.50 / Gb, we will be all in... If it is \$6 / Gb, who is paying for that?" There is a question of how much more utility researchers will get out of lower costs. The switching cost will not be trivial. The Roche system is a different workflow, it is a different process for how to batch samples, and library prep will need to be factored in.
- Illumina said it is early to speculate on Roche's system, but highlighted their capabilities with end to end workflows. From sample/library prep to sequencing and informatics, customers are looking to buy the whole ecosystem.
- PacBio stands by the comprehensiveness of their genomes, and the read length advantage of HiFi. Roche's Simplex reads can be 1Kb+ in length (vs 15-20Kb for PacBio), which the company thinks is too short to get through the full isoform for RNA applications.

Fig. 6: Roche's Sequencing and Synthesis Instruments – Note: Sequencer on Right INCLUDES Box on the Bottom



Source: Roche, Nephron Research

Fig. 7: Comparison of NGS Performance Specs

| Company                                     | Roche SBX               | Illumina                  | Ultima Genomics         |                         | PacBio                  |  |  |
|---|-------------------------|---------------------------|-------------------------|-------------------------|-------------------------|--|--|
| System                                      | "Sequencing Instrument" | NovaSeq X Plus            | UG100                   | Solaris Boost           | Revio                   |  |  |
| System Price                                | "Competitive"           | \$1.25mm                  | \$1.50mm                |                         | \$599K                  |  |  |
| Reads                                       | 15 Bn                   | 52 Bn                     | 6-8 Bn                  | 10-12 Bn                | N/A                     |  |  |
| Length                                      | 200-300 Duplex          | 2x150                     | 1x300<br>>85% Q30       |                         | 15000-20000             |  |  |
| Quality                                     | Q39 Duplex WGS          | >85% Q30                  |                         |                         | 90% Q30                 |  |  |
| \$/Gb                                       | "Competitive"           | \$2                       | \$1                     | \$0.80                  | \$8                     |  |  |
| Data Generation                             | 8Tb                     | 8Tb (x2 for 2 flow cells) | 2.4Tb (x2 for 2 wafers) | 3.6Tb (x2 for 2 wafers) | 120 Gb (x 4 SMRT cells) |  |  |
| Time  | 4 Hours                 | 48 Hours                  | 12-14 Hours             | 6 Hours                 | 24 Hours                |  |  |
| Size  | TBA                     | 34.0" x 36.7" x 62.5"     | 52.7" x 33.9" x 76.7"   |                         | 36.5" x 36.0" x 68.7"   |  |  |
| Weight                                      | TBA                     | 1,253lb                   | 1,896lb                 |                         | 1,025lb                 |  |  |
| Source: Company Documents, Nephron Research |                         |                           |                         |                         |                         |  |  |

#### Illumina: Focus is on Multi-omics, Pipeline Seems Early

Illumina was the Gold sponsor at AGBT. CEO Jacob Thaysen and team had a major focus on multiomics, highlighting a new Illumina Spatial Technology and Illumina Connected Multiomics. This was in addition to other pipeline products (Constellation, single cell, Illumina Protein Prep, and a 5-base solution for methylation). Many of these new products are early in their development, which differs from the Illumina of old where color on the pipeline was hidden until products were ready for commercialization. Illumina is under investor pressure to show progress on R&D to justify current levels of spend. We think the disclosure shift might be related to a few factors. The Bull view is that Illumina is excited about the prospects for their pipeline, and in the spirit of transparency is sharing more with investors and customers to keep them engaged. The more skeptical view is that there is increasing competition in the market, and promising these new products before they are complete will potentially stall customers from evaluating alternatives.

Before looking at the key updates, we did want to flag Illumina's commentary on the China market (7% of sales) and the Unreliable Entity List. The company's last update was with 4Q24 earnings, which came within a couple of days of the announcement. Illumina stated that they are still able to sell into the region. They've had a lot of dialogue with Chinese customers, some of which want to make sure Illumina can stay in China from a clinical studies perspective. Illumina stated that they have multiple conversations with the appropriate authorities, and will continue the dialogue. As a reminder, MGI seized the moment to announce a trade-in program for Illumina sequencers. Via Google Translate, "To help users control costs and achieve smoother platform switching, starting today, MGI will provide discounts on compatible devices or reagents based on the user's replacement model and startup frequency, and offer free trials and demo experiences." The replacement plan is also described here.

Onto the pipeline... CEO Jacob Thaysen pointed to Constellation as the pipeline product he's most excited about. "It completely sets us apart" from competitors, and Illumina thinks it will become the standard in germline testing. The crux of the technology comes from a combination of engineering and bioinformatics breakthroughs within Illumina. Unfragmented high molecular weight DNA is floated across the surface of the flow cell, clinging onto neighboring wells. Illumina can then sequence all of the information from the clusters, and also generate spatial information of the associations between clusters bioinformatically.

In essence, Illumina has created a long-read sequencing approach on their existing flow cells. The workflow is relatively simple, with 10 minutes of library prep prior to putting it onto the sequencer. Data analysis is generated with DRAGEN. This is far from a full replacement of existing long read technology, but it does chip away at the value proposition for PacBio/ONT. Early access is expected in 1H25 (vs 1Q25 prior), with a launch targeted in 2026. So far, there have been >1000 internal sequencing runs performed and >50 early access sites engaged (vs 10+ prior disclosure).

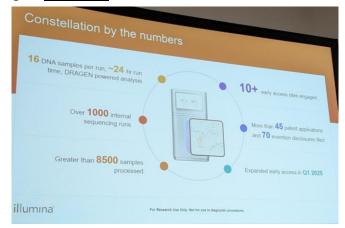
Customer feedback is that price will be important. Illumina's deck discussed pricing in the hundreds of dollars, but we believe that is dependent on multi-plexing which hasn't been finalized yet. Given unfragmented DNA is being introduced into the flow cell, there is currently no ability to barcode the sample and multi-plex. Thus, you can only run one sample per lane on the flow cell – meaning a whole genome cost would be around \$2K otherwise (barring discounting). One researcher commented to us that, "Constellation is unlikely to become the default unless they made it invisible cost wise." We also think the applications could be niche (vs becoming the standard for all samples). Comprehensive variant calling is important for things like rare disease, which is a smaller portion of the market. Broader payor coverage and reimbursement could help drive adoption.

Fig. 8: AGBT 2025: Constellation Disclosures



Source: Company Documents, Nephron Research

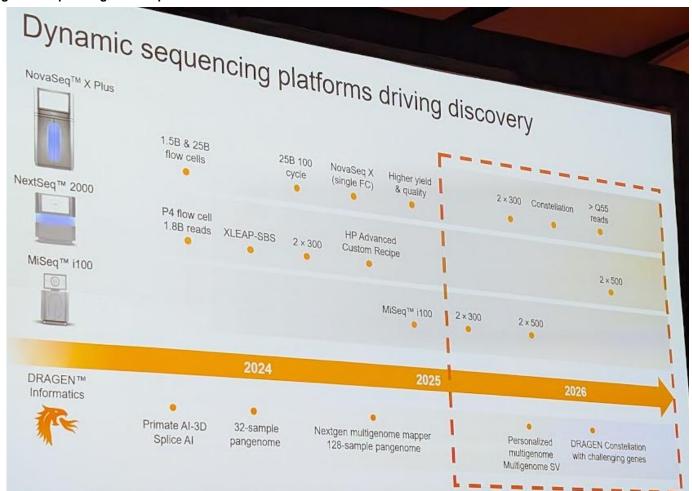
Fig. 9: ASHG 2024: Constellation Disclosures



Source: Company Documents, Nephron Research

Other sequencing pipeline products include longer reads (2x300 on the NovaSeq X+, 2x500 on benchtop systems) and also the promise of >Q55 reads (could be useful in MRD applications):

Fig. 10: Sequencing Roadmap from Illumina



On Illumina's Spatial Technology, the company had a few KOLs discuss their experience and also highlighted a product concept illustration below. The system offers whole transcriptome profiling, promising a larger tissue area (9x), higher resolutions (4x) an lower cost per unit (4x) relative to "Company T" (10x Genomics). Data presented was from fresh frozen samples (in early access), while an FFPE solution is in development. The workflow consists of tissue pre, histology on traditional imaging platforms (like Leica), spatial library prep, sequencing and then data analysis.

Fig. 11: Illumina Spatial Technology Product Concept



Source: Company Documents, Nephron Research

#### UK Biobank: Outlines Why Olink and Ultima Were Picked

Dr. Chris Whelan, Director of J&J Innovative Medicine, hosted an interesting discussion to describe why the UK Biobank Pharma Proteomics Project selected Olink (over Somalogic/Standard BioTools) and Ultima (over Illumina). As a reminder, the pilot project was founded in November 2020 and began in April 2021 with Olink. The pilot consisted of >54K participants, with results published in three Nature papers in October 2023. In a session hosted by Olink later in the day, they disclosed that these papers have had >137K accesses, and >500 references.

Based on the success of the pilot, in January 2025 the UKB-PPP consortium announced a cohort-wide study of up to 600K participants using Olink Explore HT with samples sequenced on Ultima UG 100 sequencers at the Regeneron Genetics Center (RGC).

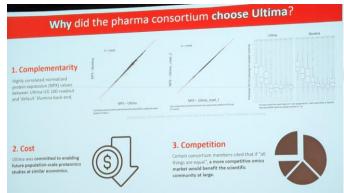
On the decision to choose Olink (over Somalogic): It was a competitive bidding process. Olink was considered slightly more attractive, but the group's final vote was "tied" on the major selection criteria. Olink's cost was considered "considerably lower," and the data had a "proven track record" as part of the pilot project. What broke the tiebreak was that the voters in favor of Somalogic were willing to switch over to Olink, while fewer Olink voters were willing to switch to Somalogic. We think the researchers that started the pilot with Olink wanted to have consistency in the data source.

On the decision to choose Ultima (over Illumina): The read-out is a counting application using sequencing on the back end. Results between Illumina and Ultima were considered highly correlated, with a .983 CV. "The precision was nearly identical." The cost was very attractive from both companies, though Ultima was committed to setting an equal price for future projects. What pushed the decision towards Ultima was that "All things equal, the consortium wanted competition with Illumina to get more innovation."

Fig. 12: "Why did the pharma consortium choose Olink?"



Fig. 13: "Why did the pharma consortium choose Ultima?"



Source: Nephron Research

Source: Nephron Research

# Ultima Highlights Greater Throughput w/ Solaris, Progress in MRD w/ LH

While there was a lot of focus on Roche and Illumina at AGBT 2025, we think Ultima continues to make a lot of progress. Last year, Ultima commented that it had a low-to-mid teens number of customers in early access. Today, that number has doubled – with a strong hit rate on the top 25 sequencing accounts. Ultima has highlighted two high profile research wins with the UK Biobank and Chan Zuckerberg, demonstrating their high-throughput capabilities. We thought the highlight from their AGBT presentation though was progress in MRD with LabCorp, who highlighted data in colorectal cancer using Ultima's ppmSeq solution.

In terms of updates, Ultima announced "Solaris" – which increases the throughput researchers can get off of the UG 100 system. Solaris works best for shorter read applications, like proteomics, single cell and others. The "Boost" is improved amplification and shorter libraries, which enables faster sequencing times. It is currently up and running at 2 early access sites (including the Broad Institute). The punchline is that Solaris Boost takes sequencing up to 100bn reads per day. There is a 50%+ increase in output (10-12bn reads), with the equivalent of >30K genomes per year. The throughput increase drops the cost for sequencing to \$0.24 per million reads. The math is up to 12bn reads per wafer, 2 wafers running at once at a 6 hour run time (so 8 wafers per day). The Broad Institute described the increased throughput as "more of a scheduling exercise." Boost Mode would support a massive amount of data generation.

Affordable sequencing is here with Solaris 10-12B 6-8B 50%+ increase in output reads per wafer UG 100 Solaris More than 30,000 Up to 20,000 genomes per year genomes per year \$0.24 \$0.30 20% decrease in cost 30x WGS SNVQ60 2ng input of cfDNA ppmSEQ 20% decrease in cost genome genome ULTIMA Note: cost at list price over 4 wafers; at 100Gb/genome Note: SNVQ = SNV Quality Score GENOMICS 14 For Research Use Only. Not for Use in Diagnostic Procedures.

Fig. 14: Illumina Spatial Technology Product Concept

Source: Company Documents, Nephron Research

LabCorp presented some MRD data highlighting the analytical performance of their test using Ultima's UG 100. LabCorp's ideal MRD assay has high performance (sensitivity, specificity), rapid turnaround time to impact clinical decision making, and is scalable from a cost perspective. LabCorp ran a pilot study in Ultima's service lab with 5 samples per wafer, and then processed their own samples in house with 6 samples per wafer. Solaris significantly increased coverage, with median coverage of 86.3x (vs 38.7x in the pilot). For MRD where you are looking for a needle in a haystack, Solaris allowed for much greater sequencing depth at a decreasing cost per sample. LabCorp also highlighted the signal-noise ratio, with 99% specificity notably at 2.9ppm.

Fig. 15: Solaris Boosted Median Coverage from 39x to 86x

The assay needs to get sufficient sequencing depth to enable ctDNA detection in a way that is scalable and affordable

We compared the mean coverage across cfDNA samples from non-diseased donors to assess sequencing depth

Pilot study: 5 samples per wafer, processed at Ultima

Solaris: 6 samples per wafer, processed at Libcorp

Solaris showed significantly higher overall coverage relative to previous versions

Pilot median coverage: 38.7x

Solaris median coverage: 86.3x

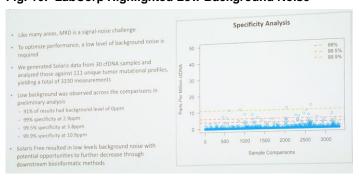
Solaris median coverage: 86.3x

Solaris neglator coverage: 86.3x

Source: LabCorp, Nephron Research

increasing throughput and decreasing cost per sample

Fig. 16: LabCorp Highlighted Low Background Noise



Source: Nephron Research

## Element Bio: Innovation Roadmap Ahead of AGBT

**Element Bio's presence was relatively light (by design) at AGBT 2025**. We had the chance to catchup with co-founder and CTO Mike Previte and CFO Logan Zinser on the ground.

Element recently hosted a <u>2025 innovation roadmap</u> to highlight what is ahead, with a large focus on AVITI24. AVITI24 is an integrated sequencing and single cell multiomics platform solution. The system was originally introduced at AGBT 2024, is with customers in early access, and will begin shipping commercially later this year.

AVITI 24 combines multiomics analysis and sequencing in cells. AVITI24 enables Q50 read quality, and also higher throughput with up to 3bn reads (2x150 read length). With 1 run a day (24 hour run time), at 20 working days, the company quotes the ability to run 50-90mm cells per month. In 1 month of operating AVITI24, Element Bio highlighted that users can run drug screens (1440 compounds, 1000s of cells per compound), CRISPR Screens (120K gene perturbations), and immune repertoire (100+mm PBMCs profiled).

As a reminder, Element is not positioning AVITI24 as a spatial technology. In 24 hours, researchers can get cell morphology data, RNA reporting, protein/phosphorylated, in vitro 3D ABC sequencing with <45 minutes of hands on time.

AVITI has a list price of \$289K, and we think the AVITI24 solution is higher – potentially around \$400K. Relative to AVITI, the AVITI24 system has advancements in computing power and AI image analysis, applying ML to make the analysis fast and high performing.

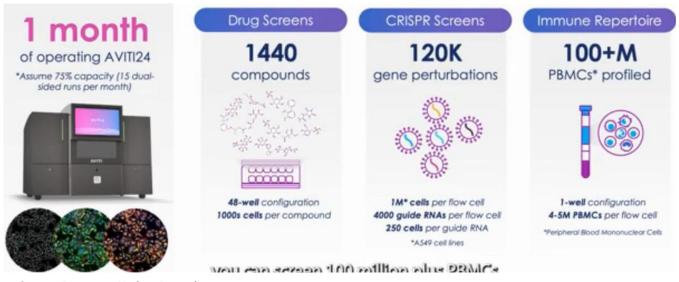
Fig. 17: AVITI24 Metrics

# **AVITI24: Leading a Revolution**

The First and Only Integrated Sequencing and Single Cell Multiomic Platform Solution



Fig. 18: AVITI24 Metrics

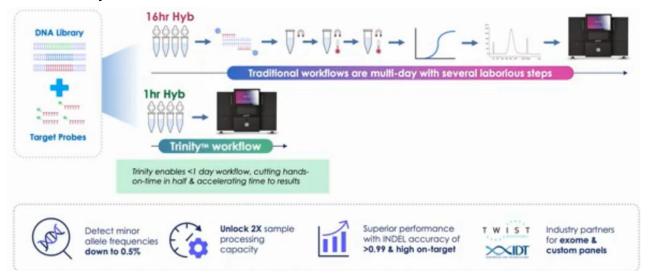


Source: Company Documents, Nephron Research

Element also highlighted their Trinity workflow (introduced at AGBT 2024), which streamlines targeted sequencing – removing the very complex steps. Typically, workflows start with a DNA library, there is probe hybridization, bead binding, washing steps, post-hybridization amplification, library QC then sequencing. Trinity streamlines this to just the DNA library, probe hybridization and sequencing. The approach removes PCR amplification steps, significantly reducing hands on time.

The initial focus is on exome sequencing, but the system is compatible if customers would like to do more. Any compatible panel based on DNA probes from Twist or IDT is compatible. Future endeavors will push into targeted/custom panels. Trinity Plus will be released in 2025 for an enrichment workflow for areas of interest. One area of focus is on agriculture – using corn as an example, a subset of 50 markers could get genotyped with high accuracy combined with low pass sequencing. Other opps highlighted include low pass human sequencing (exomes at deeper coverage), infectious disease and MRD.

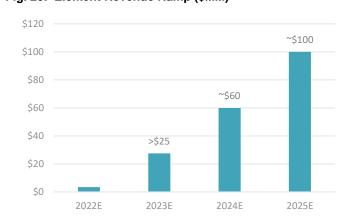
Fig. 19: Element Trinitiy Workflow



As a reminder, Element highlighted updated financial statistics earlier this year. The cumulative installed base was >2.4x from 112 at the end of 2023, which implies an ending installed base of ~270 systems. Element had disclosed >210 installations of AVITI in an early Sept conference, and >190 in a press release on 7/11/2024. Element disclosed 15 AVITI24 systems installed in December 2024 (first began shipping), 60% of customers new to Element. The company added that they had double that number in terms of orders at year end. We think a reasonable bogey for 2025 is if around 1/4 of total AVITI shipments used the AVITI24 configuration.

We continue to look for an update on a high-throughput offering in late 2025/early 2026. While Element is limited today to the benchtop, the #1 ask from customers is for a high-throughput solution - and we think it is likely #1 on Element's new product roadmap. The feedback on Element's data quality has been very good, and the error profile is most similar to Illumina's amongst the competition. Higher scale would enable researchers to super-size the work they are doing today with AVITI24 through a research lens. It could also offer up opportunities to transition larger Illumina customers who want to drive competition in the sequencing market and also take advantage of Element's quality/cost.

Fig. 20: Element Revenue Ramp (\$MM)



Source: Company Documents, Nephron Research

Fig. 21: Element Installed Base and Order Trends



Source: Company Documents, Nephron Research

#### Bruker: Interesting Science, Tough End Market Exposure

Bruker was the third Silver sponsor at AGBT 2025, and we had the opportunity to interact with CEO Frank Laukien and President of Bruker Nano Mark Munch. Bruker highlighted a number of the super interesting research Tools that the company has consolidated into their Bruker Spatial Biology unit, notably including the legacy NanoString business. The key question is whether this can become a good business for investors given the margin profile and tough end market backdrop.

In the analyst session hosted on Wednesday afternoon, CEO Frank Laukien weighed in on customer sentiment. Within academic and government (around 40% of sales), approximately 25% is in the US (around 10% of sales). Of this, about half is with the NIH, while the rest is spread across other sources (including the NSF, NASA, etc). In the US, "There is some turmoil and uncertainty... but it is not all doom and gloom." Laukien acknowledged some of the uncertainty, and whether this could just blow over in the next few weeks or something new could emerge. Bruker's portfolio is predominantly capital equipment (around 70%), which is the area that academic customers have expressed to us the greatest spending concerns. In the short term, Bruker thinks their backlog can help them navigate the uncertainty (though that wasn't the case for several quarters in 2024). In terms of seasonality,

about half of sales in the quarter come in the 3<sup>rd</sup> month. About 25% are in the first month, and 25% in the second month.

CEO Laukien also commented that they are likely not interested in acquiring assets in the sequencing space. At AGBT, a recurring theme was around multi-omics, with several sequencing companies pushing into spatial-like technologies (Illumina, Element, Singular most notably). While Bruker has not been afraid of doing controversial acquisitions to add new capabilities, Laukien pointed to NGS as being very competitive, and many of the potential targets are not close to making money.

The highlight of Bruker's new offerings was the PaintScape system, for direct visualization of the 3D genome. Leveraging jebFISH technology, researchers can get direct visualization of the genome architecture and chromosomal structure of individual single cells with ultra-high spatial resolution. This includes visualization and analysis of ploidy variation, chromatin folding conformations, and compactness in single cells that can reveal clues about disease. The system will launch sometime in July/August. Bruker highlighted interest from a handful of customers at the event.

Fig. 22: Bruker PaintScape Value Proposition BRUKER Understanding 3D genome organization gives new insights into mechanisms of disease including cancer Dysregulation of Aberrations of cellular programs genome organization gene expression (transcription) DNA replication genome organization studies cell division 100 南西 Visualization and analysis of ploidy variation, chromatin folding Aberrant p- and q- arm conformations, and compactness of chromosome structure Aberrant Disrupted chromosom misfolding ploidy changes individual homologs in single cells car reveal clues to mechanisms of cancer مرونالي مرالته التناراتين initiation and progression mill .... Subpopulations of cells Novel proximities of genomic Disruptions of with novel loci proximities A/B compartments & TADs openness and folding

Source: Company Documents, Nephron Research

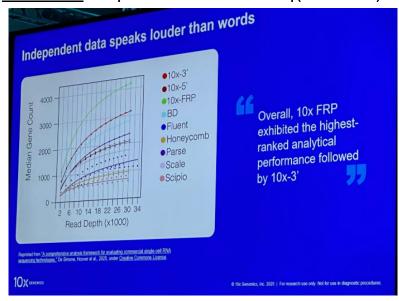
# 10X Genomics and Other Single Cell/Spatial Tech

On Sunday, 10x Genomics hosted a workshop discussing its key technology platforms (Chromium, Visium, and Xenium), new products, efforts to enable large-scale single cell analysis, and reduce costs per cell and per experiment. We found the upcoming launch of Xenium RNA+Protein Multiomics as the most significant update.

#### **Key Takeaways**

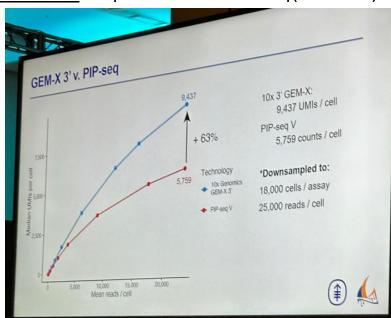
 Competition – As competition has increased, the competitive intensity in single cell & spatial has increased. 10x has demonstrated in several independent head-to-head analyses its performance advantages over competitors.

Fig. 23: 10x Genomics: Comparison of GEM-X 3' to PIP-seq (Fluent / ILMN)



Source: Company Documents, Nephron Research

Fig. 24: 10x Genomics: Comparison of GEM-X 3' to PIP-seq (Fluent / ILMN)



- Xenium advantages over other spatial technologies
  - o <u>A Comparative Analysis of Imaging-Based Spatial Transcriptomics Platforms</u>

- o <u>Systematic Benchmarking of High-Throughput Subcellular Spatial</u>
  <u>Transcriptomics Platforms</u>
- Systematic benchmarking of imaging spatial transcriptomics platforms in FFPE tissues
- Comparison of imaging-based single-cell resolution spatial transcriptomics profiling platforms using formalin-fixed, paraffin-embedded tumor samples
- Strategic focus maximize biological insight
  - More biology more analytes, applications, higher resolution, sensitivity, multiplexing, and more scale and throughput.
  - Easier to use workflow robustness, logistics, automation, sample prep, and data analysis and visualization.
  - Lower costs lower cost per cell, tissue area, sample, experiment; 10x expects to continue to drive costs down through innovation on its long-term roadmap.

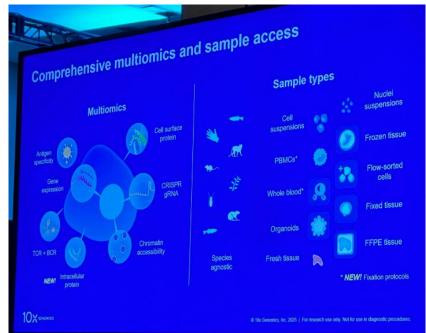


Fig. 25: 10x Genomics: Comprehensive multiomics and sample access

- Opportunity to expand into translational and preclinical studies
  - Examples of translational cohort studies:
    - Owkin, Inc Spatial multiomics dataset from 7,000 patients from the identification of new disease biology, patient subtypes, biomarkers, and drug types.
    - Garvan Institute of Medical Research Mapping 50mm human cells from 10k people to identify unique genomic fingerprints of autoimmune diseases, heart diseases, and cancer with GEM-X

 Foundation for the National Institutes of Health – Evaluating thousands of tumor and immune samples to find biomarkers of progress from early precursor conditions to multiple myeloma

- CURE Profiling samples from over 1k long-term survivors in hard-totreat cancers with Visium HD
- Agency for Science, Technology and Research (Singapore) A cellular, location based approach for disease biomarker analysis to accelerate drug discovery efforts using AI to infer cell-to-cell interactions from spatial data of thousands of samples.
- The Francis Crick Institute Consortium of universities, hospitals and industry to study 6k cancer patients and determine why certain patients respond to immunotherapy while others do not.
- SCRUM-Japan MONSTAR-SCREEN consortium MONSTAR-SCREEN-3 includes multiomics analyses, including whole-genome sequencing and spatial single-cell transcriptome analysis (including Xenium).

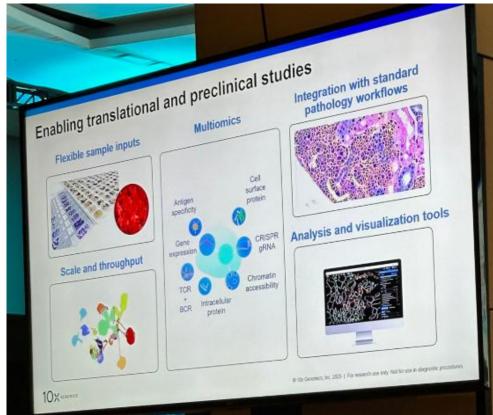


Fig. 26: 10x Genomics: Enabling translational and preclinical studies

Source: Company Documents, Nephron Research

#### • New capabilities

- Visium HD Whole transcriptome probe assay using FFPE, Fresh Frozen and Fixed Frozen sample types, 3' assay, cell segmentation analysis, and larger capture area.
- Xenium RNA+Protein Multiomics

RNA and protein on one slide with one workflow Integrated data visualization Fully automated multi-analyte decoding Visualize both analytes Sample prep with Xenium Explorer Automatic read out as part of Xenium run Integrates seamlessly with RNA panel sample preparation Adds ~1 day to run Adds <1 hour to workflow Protein stain detection Up to 7 cycles, 4 markers per cycle © 10x Generals; Inc. 2025. J. For research use only. Not for use in diagnostic procedures

Fig. 27: 10x Genomics: Workflow for Xenium RNA+Protein

Source: Company Documents, Nephron Research

**Scale Biosciences (private)** – Founded 2 years ago, Scale Biosciences has seen customer adoption and has expanded its portfolio to compete in multiple single cell verticals.

Transcriptomics

- QuantumScale SC RNA
- ScaleBio SC RNA
- ScaleBio SC RNA
2024
- ScaleBio SC Targeted Methylation
- Tagmentation Toolkit

- Transcriptomics

Proteomics

- Perturbomics

- ScaleBio SC CRISPR
2024
- ScaleBio SC Targeted Methylation
- Tagmentation Toolkit

- Tagmentation Toolkit

- ScaleBio SC RISPR
2024
- ScaleBio SC CRISPR
2024
- ScaleBio

Fig. 28: Scale Biosciences: Product Portfolio

One Flexible Platform, For Any Scale Extra **Small Medium** Large 8-2,304 8-2,304 8-9,216 Modular 8-9,216 ScalePlexed **ScalePlexed** 1-96 Samples 8-9,216 ScalePlexed 85K 168K 2M 4M 0.8¢/cell 3.5¢/cell 1.0¢/cell 5.6¢/cell SCALE

Fig. 29: Scale Biosciences: Pricing based on volume

Source: Company Documents, Nephron Research

**Parse Biosciences (private)** – Parse believes its solutions can expand applications in single cell, including:

- 1. High-throughput drug and target screens
- 2. Building datasets to train AI models
- 3. Clinical trial and population studies

Validating Parse's Superior Performance

Genomics

A risk-reward examination of sample multiplexing reagents for single cell RNA-Seq

"The library sizes and number of detected genes were approximately five fold higher in Parse Biosciences when downsampling to an equivalent number of reads per library."

"Consistent with the manufacturer's specifications, the cell doublet rate was an order of magnitude lower for Parse Biosciences."

"Souporcell estimated an ambient RNA content of 29.97% for droplets"

Brown et al, 2024

PARSE BIOSCIENCES

Fig. 30: Parse: Performance Validation

#### Important Disclosures, Disclaimers and Limitations of Liability

Certification. The views expressed herein reflect the personal views of the research analyst(s) on the subject securities or issuers referred to. No part of any Nephron Research LLC ("Nephron") research analyst's compensation is or will be directly or indirectly related to the specific recommendations or views expressed.

This publication has been reviewed by Nephron in order to verify compliance with Nephron's internal policies on timeliness, against insider trading, disclosures regarding ratings systems, conflicts, and disciplinary matters.

As a categorical matter, Nephron Research has a policy of covering all issuers underwritten by NCMG LLC.

No Advice or Solicitation. Nephron is an independent research provider and is not a member of the FINRA or the SIPC and is not a registered broker-dealer or investment adviser. The reader acknowledges the following: (1) you are capable of making your own investment decisions and are not doing so in reliance of the content provided in this document; (2) neither Nephron or any individual author of this material is recommending or selling any securities to you; and (3) the content contained herein has not been tailored to any person's specific investment objectives and is not intended or provided as investment advice.

The information contained herein is not intended to be an inducement, invitation or commitment to purchase, provide or sell any securities, or to provide any recommendations on which individuals should rely for financial, securities, investment or other advice or to make any decision. Information herein is for informational purposes only and should not be construed by a potential subscriber as a solicitation to effect or attempt to effect transactions in securities, or the rendering of personalized investment advice for compensation. Nephron will not render specific investment advice to any individual or company and the content contained herein has not been tailored to the individual financial circumstances or objectives of any recipient. The securities and issuers discussed herein may not be suitable for the reader.

Nephron recommends that readers independently evaluate each issuer, security or instrument discussed herein and consult any independent advisors they believe necessary prior to making any investment decisions. Investment decisions should be made as part of an overall portfolio strategy and you should consult with professional financial, legal and tax advisors prior to making any investment decision.

For Informational Purposes Only. This publication is provided for information purposes only, is not comprehensive and has not been prepared for any other purpose. All information contained herein is provided "as is" for use at your own risk. The views and information in this publication are those of the author(s) and are subject to change without notice. Nephron has no obligation and assumes no responsibility to update its opinions or information in this publication. The information contained in this publication whether charts, articles, or any other statement or statements regarding market, stocks or other financial information has been obtained from sources that Nephron believes to be reliable, however Nephron does not represent, warrant or guarantee that it is accurate, complete or timely. Nothing herein should be interpreted to state or imply that past results are an indication of future performance.

Rating System. Nephron uses an absolute rating system which rates the stocks of issuers as Buy, Sell, or Hold (see definitions below) backed by a 12 Month price target. Each analyst has a single price target on the stocks that they cover. The price target represents that analyst's expectation of where the stock will trade in the next 12 months. Upside/downside scenarios, where provided, represent identified potential upside/potential downside to each analyst's price target over the same 12-month period. Buy - Current stock price generally represents upside to our 12-month price target of 20%+. Hold - Current stock generally represents limited opportunities on both the long and short side over 12-month period.

The entire contents of this publication should be carefully read, including the definitions of all ratings. No inferences of its contents should be drawn from the ratings alone. Disclaimer Regarding Forward Looking Statements. The information herein may include forward looking statements which are based on our current opinions, expectations and projections. All ratings and price targets are subject to the realization of the assumptions on which analyst(s) based their views. The assumptions are subject to significant uncertainties and contingencies which may change materially in response to small changes in one or more of the assumptions. No representation or warranty is made as to the reasonableness of the assumptions that contributed to the rating or target price or as to any other financial information contained herein. Nephron undertakes no obligation to update or revise any forward looking statements. Actual results could differ materially from those anticipated in any forward looking statements. Nothing herein should be interpreted to state or imply that past results or events are an indication of future performance.

IRS Circular 230 Prepared Materials Disclaimer. Nephron does not provide tax advice and nothing contained herein should be construed to be tax advice. Please be advised that any discussion of U.S. tax matters contained herein (including any attachments) (i) is not intended or written to be used, and cannot be used, by you for the purpose of avoiding U.S. tax-related obligations or penalties; and (ii) was written to support the promotion or marketing of the transactions or other matters addressed herein. Accordingly, you should seek advice based on your particular circumstances from an independent tax advisor.

No Warranties. Nephron disclaims to the fullest extent permitted by law any warranties and representations of any kind, whether express or implied, including, without limitation, warranties of merchantability or fitness, for any purpose and accuracy or for any other warranty which may otherwise be applicable or created by operation of law, custom, trade usage or course of dealings. Nephron makes no representation that (i) the content will meet your requirements, (ii) the content will be uninterrupted, timely, secure, or error free, or (iii) the information that may be obtained from the use of the content (including any information and materials herein) will be compliant, correct, complete, accurate or reliable. THERE ARE NO WARRANTIES EXPRESSED OR IMPLIED, AS TO ACCURACY, COMPLETENESS, OR RESULTS OBTAINED FROM ANY INFORMATION.

Disclaimer of Liability. We shall not accept any liability with respect to the accuracy or completeness of any information herein, or omitted to be included herein, or any information provided, or omitted to be provided, by any third party. We shall not be liable for any errors or inaccuracies, regardless of cause, or the lack of timeliness, or for any delay, error or interruption in the transmission thereof to the user. TO THE FULLEST EXTENT PERMITTED BY LAW IN YOUR JURISDICTION, IN NO EVENT SHALL NEPHRON BE LIABLE FOR ANY DIRECT, INDIRECT, CONSEQUENTIAL PUNITIVE, SPECIAL OR INCIDENTAL OR OTHER DAMAGES ARISING OUT OF THE CONTENT.

Reproduction and Distribution Strictly Prohibited. © Copyright Nephron Research LLC. No part of this publication or its contents may be downloaded, stored in a retrieval system, further transmitted, or otherwise reproduced or redistributed in any manner without the prior written permission of Nephron. The contents herein are directed at, and produced for the exclusive use of Nephron clients and intended recipients. No license is granted to Nephron clients and/ or the intended recipient Nephron will not treat unauthorized recipients of this publication as its clients.