Spatial Biology Market Report
First Edition: 2022

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DeciBio

Agenda

- **Introduction & Methodology**
- **Executive Summary**
- **Market Analysis**
- **Publication Analysis**
- **Primary Market Research**
- **Competitive Analysis**

DeciBio Spatial Market Report 2022 - Introduction

Purchase Overview

Thank you for your purchase of DeciBio's Spatial Biology Market Report. This report provides a summary of the current spatial biology market landscape as well as a forward-looking perspective of the spatial biology market from 2022 to 2027. Content includes a rigorous assessment of industry market size and growth, as well as key drivers, moderators, and trends. In addition, we provide detailed segmentation by technology, customer type, application, plex level, competitor, and geography.

This report was informed by a comprehensive primary and secondary research campaign, as well as the insights and expertise of DeciBio's experienced consultants, who monitor, evaluate, and assess the market on an ongoing basis.

Every purchase of our market reports comes with 1 hour of DeciBio team time, affording the customer the opportunity to have the report author present report highlights and answer questions for the licensed customer. To arrange your presentation time, please email us at rebecca.burnham@decibio.com.

For any questions or inquiries related to custom market research or strategy consulting engagements in the spatial biology space (or beyond), please feel free to reach out to Colin Enderlein (Enderlein@decibio.com) and Cameron Braverman (Braverman@decibio.com).

This report was authored by a DeciBio team with extensive knowledge of the spatial biology and broader precision medicine markets

About the Authors

Cameron Braverman
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As a Senior Associate at DeciBio, Cameron has overseen 300+ expert interviews with KOLs in the spatial biology field and has been a part of numerous competitive intelligence and strategy projects for top players in the field. In addition to authoring the spatial report, Cameron manages the DeciBio spatial biology Q&A blog series.

Rebecca Burnham
Associate Product Manager | Ph.D.

As an Associate Product Manager at DeciBio, Rebecca has authored multiple market research reports, covering a variety of topics in the life sciences space including liquid biopsy, life science research tools, and spatial biology. In addition to the market reports, Rebecca manages the MarketBooks, which tracks revenue for 100+ companies in the genomics, proteomics, and cellomics markets.

Colin Enderlein
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As a Senior Project Leader at DeciBio, Colin has overseen DeciBio's pharma and clinical diagnostics verticals, conducting numerous projects on biomarker and Dx development and commercialization. He has conducted global studies on oncology Dx market access, through which he has gained insights on multiple regulatory & reimbursement systems. Colin has backgrounds in tech transfer, preclinical translational research, and CDx strategy at NanoString.

Andrew Aijian
Partner | Ph.D.

As a Partner at DeciBio, Andrew specializes in the development, commercialization, and utilization of research tools and diagnostics across the entire precision medicine spectrum, from early discovery through the patient journey. Andrew works to reduce the barriers to innovation between precision medicine stakeholders. At DeciBio, Andrew has a particular focus in oncology biomarkers and diagnostics and has led dozens of consulting engagements with leading companies in this space.

DeciBio forecasts the WW Spatial Biology market to grow at 30% p.a., reaching ~$1.2B in 2027

Spatial Biology Market Report Abstract

This report provides an overview of the spatial biology market from 2022 to 2027. The spatial biology market, as defined in this report, is comprised of revenue from instruments and reagents sold to academic, biopharma, and CRO customers, along with service revenues generated by CROs and reference labs. This market is moderately consolidated today, with the top vendors including 10X Genomics, NanoString, and Akoya Biosciences making up ~50% of the market, however, multiple other mid-sized and smaller-sized players (e.g., Standard BioTools, Leica Microsystems, Ultivue, and Vizgen) are poised to capture share are the market grows and evolves.

For this report, we leverage a combination of secondary research (e.g., analysis of quarterly and annual reports, earnings call transcripts, clinical trials, congress abstracts, company websites, etc.) and primary research (e.g., 23 interviews with key spatial biology stakeholders from academia, biopharma, and leading specialty CROs) to assess the current and expected future adoption and utilization of spatial biology tools and technologies, and to characterize the key market dynamics. From our research and analysis, we estimate that the spatial biology market is ~$320M in 2022 and is expected to grow 30% p.a. in the next 5 years, to reach ~$1.2B by 2027.** Our analysis indicates continued market growth within academia and rapid expansion in use by biopharma and CROs, particularly for use within clinical trials.

For each of the subsegments analyzed, we present forecasted data from 2022-2027. In addition, we detail market drivers (e.g., increased adoption in certain customer segments) and moderators (e.g., high cost of instruments and reagents), market trends (interest in combining spatial transcriptomics with proteomics), a high-level customer breakdown (academia, large pharma, small pharma, CROs), and offer key information on top competitors.

All analyses are based on publicly reported data and DeciBio research and analysis.*

Notes: * Disclaimer: Some of the companies listed in this report may be DeciBio Consulting clients and customers; ** We do believe that uncertainty to these forecasts exist (potential range: 20-45% p.a.), considering that the field is relatively young and pivotal developments may occur within the forecasted period that could determine future adoption of the technology.
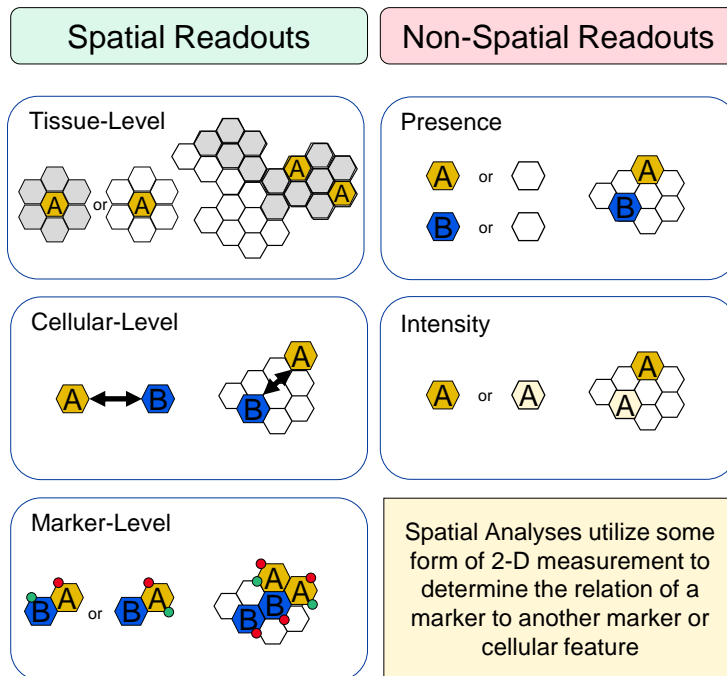
Source: DeciBio Analysis

Spatial biology provides a new dimension of biological insight to tissue analysis which can be leveraged to develop better therapeutics and diagnostics

What is spatial biology?

- Spatial Biology can be defined as the **analysis** of a target analyte(s) in tissue in a spatial context (i.e., the expression of the marker in context to its location within the tissue and/or other markers)
  - Spatial analysis provides for a more nuanced understanding of the interactions / biology within the tissue microenvironment
- Spatial biology is often (though not exclusively) driven by **multiplex analysis** of biomarkers and enabling technologies, e.g., mIF, mIHC, spatial transcriptomics, multiplex FISH, imaging mass cytometry, and others
- Today, most spatial analyses are **proteomic** or **transcriptomic** (e.g., mRNA transcripts); spatial genomics (e.g., **DNA**) also exists but is less common
  - While some recent product launches and partnerships target multi-omic analyses (e.g., combined transcriptomics and proteomics)*, spatial technology utilization is primarily single-omic today
- Academia currently comprises the largest customer segment of spatial biology analysis, and in many cases their use of spatial-omics is for basic research; pharma use of spatial biology for translational / clinical studies is rapidly on the rise
  - Although pharma is utilizing spatial biology for biomarker and CDx development, the clinical utility of spatial biology has yet to be validated; as such, the technological, regulatory and payor infrastructure to support clinical use is not yet established
  - Nonetheless, clinical use of spatial technology for therapy selection is expected within 3 - 5 years

Spatial Readouts

Non-Spatial Readouts

Tissue-Level

Cellular-Level

Marker-Level

Presence

Intensity

Spatial Analyses utilize some form of 2-D measurement to determine the relation of a marker to another marker or cellular feature

Spatial technology is primarily used in basic and translational research today; it's use in clinical trials is expected to grow, with Dx applications on the horizon

Spatial Biology Applications

| <5% | Market Share, Overall Spatial Activity | >50% |

Basic Research / Discovery Research

- Basic research, typically performed by researchers in biopharma and academia, aims to address hypotheses developed to better understand biology and disease pathology
  - Examples include: understanding cellular / receptor localization, regulation, or interactions

- Research topics span various fields of study* due to relative ease of tissue collection from biobank clinical samples and animal models

- These experiments typically involve using higher plex levels (e.g. >20 markers, or whole transcriptome) to address broad questions and/or discover novel insights

Translational & Clinical Research

- Translational and clinical research, which leverage human / patient samples with ties to clinical outcomes, aims to address hypotheses specifically related to human health and treatment
  - Examples include: drug target identification, biomarker identification, therapeutic development

- Research is primarily focused in oncology (especially immuno-oncology) today

- Exploratory / discovery experiments favor high plex (>20 markers); late-stage research favors targeted, smaller panels (e.g., 2 – 6 markers)

Routine Clinical Use / Diagnostics

- For routine clinical use, a spatial technology and biomarker / signature must show robust analytical and clinical validation; a high bar requiring large trials and numerous samples, which is limited by cost and analysis requirements today

- Early data suggests a role for spatial signatures as both prognostic and predictive for therapeutic benefit

- The first spatial (C)Dx is expected to be for immuno-oncology due to relevance of spatial information in the underlying biology and pathophysiology of immuno-oncology; some assays are in early stages of development / exploration in clinical trials

This report is divided into the following sections

Table of Contents

Click on title to jump to section

1st Edition: What does it include?

Qualitative Analyses

- Analysis of the market drivers, moderators, and trends in the spatial biology market, based on interviews with experts and extensive secondary research
  - Verbatim quotes from primary research to illustrate a variety of viewpoints and experiences

- Market insights for each of the market segments analyzed, including:
  - Customer
  - Technology
  - Application
  - Plex Level
  - Competitor
  - Geography

- Deep-dive profiles of select key competitors

Quantitative Analyses

- Bottom-up market model (based on number of customers by type, and annual spend), informed by primary and secondary research (e.g., public filings)

- Market sizes for each of the market segments analyzed, including:
  - Customer
  - Technology
  - Application
  - Plex Level
  - Competitor
  - Geography

- Market forecast from 2022 - 2027

The quantitative and qualitative analysis was informed by an extensive secondary research and 23 interviews with spatial biology stakeholders

Research Methods

Primary Research

N = 23

| EU |
| U.S. |

N = 23

| Small Pharm |
| CRO |
| Large Pharm |
| AMC |

Geography   Setting
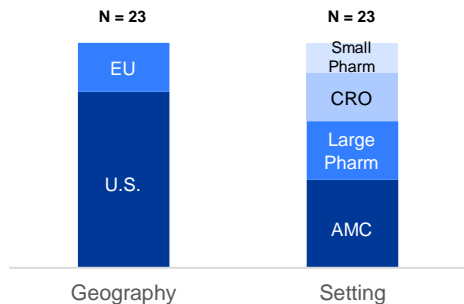
Secondary Research

Proprietary Databases / Analysis

DeciBio

- DeciBio conducted 23 interviews with various spatial biology stakeholders across the U.S., and EU to assess current and expected future utilization of spatial biology and understand preferences by technology and vendor

- DeciBio reviewed SEC filings, conference abstracts, publications, clinical trials, earnings call transcripts, press releases, funding databases, company websites, and more to capture information about assays, technologies, company roadmaps / strategies, revenues, growth projections, market trends, etc.

- DeciBio leveraged proprietary internal databases and tools, as well as our domain expertise in precision oncology, to inform quantitative and qualitative market perspectives and trends

We segmented the spatial biology market along the following 8 segments

Market Segmentation Overview

Segments	Subsegments			
Customer	• Academia	• Large Biopharma*	• Small Biopharma	• CRO
Technology	• mIF	• mIHC	• Spatial Transcriptomics	• Other^
Plex Level	• 2-3 Plex	• 4-8 Plex	• 9-10 Plex	• 20+ Plex
Analyte	• Protein	• RNA	• Other	
Application	• Basic / Discovery Research	• Translational / Clinical Research	• Routine Clinical Diagnostic	
Therapeutic Area	• Oncology • Cardiology	• Immuno-oncology • Other	• Neuroscience	• Infectious Disease
Competitor (grouped into buckets)	• 10X Genomics • Ionpath • Vizgen	• Advanced Cell Diagnostics • Leica Microsystems • NeoGenomics	• Akoya Biosciences • NanoString • Other	• Standard BioTools • Ultivue
Geography	• United States	• Europe	• Rest of World (ROW)	

Notes: * Large pharma includes only biopharmaceutical companies with revenues >$10B; ^ Other includes technologies such as Imaging Mass Cytometry, MERFISH, etc.
Source: DeciBio Analysis

This report focuses on spatial biology products and services market, with an emphasis on wet-lab, image analysis is not included in the scope of the analysis

Report Scope

Technologies and Revenues Included

- **Spatial Biology -** the study of biology and pathophysiology in which the spatial context of the analytes is taken into consideration **(including both single- and multiplex spatial analyses)**

- **Technology classes which are designed to profile and analyze multiplex biomarkers *in situ*** including includes mIF, mIHC, digital-spatial profiling, multiplex FISH, and imaging mass cytometry

- **Instrument, reagent revenues** associated with the purchase of spatial biology platforms or reagents / kits used to run the assays, and **service revenues associated with wet-lab processing of spatial slides** (e.g., by CROs / Reference Labs)

- **Sales of products and services to academic, biotech / pharmaceutical companies, and CRO customers** including both therapeutic companies and diagnostic / analytical tools companies

Technologies and Revenues Excluded

- **Digital pathology / image analysis** in which automated image analysis, algorithms, or pathologist-supported software is used to perform whole slide image analysis of any sort

  - **3rd Party Image Analysis** image analysis performed by a standalone image analysis company not included in pricing

- **Service revenue** related CDx development

- **Histology testing without spatial analyses** including multiplex assays which analyze presence or intensity of analytes only

Abbreviations used in this report

Index of Abbreviations

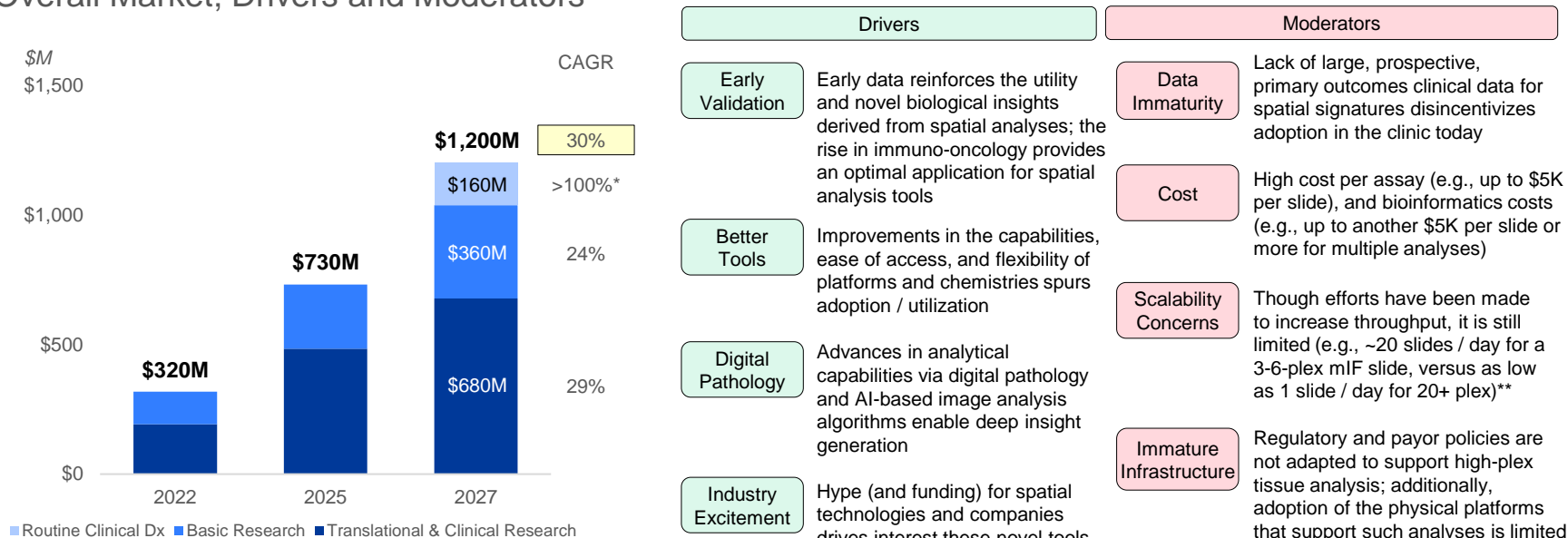| Term	Definition	Term	Definition	Term	Definition	Term	Definition	Term	Definition
Abs	Antibodies	DSP	Digital Spatial Profiler	IA	Image Analysis	ROI	Region of Interest	WW	Worldwide
AI	Artificial Intelligence	EA	Early Access	IBD	Inflammatory Bowel Disease	RRMM	Relapsed / Refractory Multiple Myeloma	MIBI-TOF	Multiplexed Ion Beam Imaging by Time of Flight
AMC	Academic Medical Center	E2E	End-to-End	IDS	Image Data Services	RUO	Research Use Only	mIF	Multiplex Immunofluorescence
AST	Advanced Solid Tumors	FF	Fresh Frozen	IMC	Imaging Mass Cytometry	smFISH	Single-Molecule FISH	mIHC	Multiplex Immunohistochemistry
CDx	Companion Diagnostics	FFPE	Formalin-Fixed Paraffin-Embedded	I/O	Immuno-Oncology	SMI	Spatial Molecular Imager	MS	Mass Spectrometry
CRC	Colorectal Cancer	FIH	First-In-Human	ISH	In Situ Hybridization	TAP	Technology Access Program	MTA	Multiplex Tissue Analysis
CRO	Contract Research Organization	FISH	Fluorescent In Situ Hybridization	LOD	Limit of Detection	TIL	Tumor Infiltrating Lymphocytes	NCI	National Cancer Institute
CSP	Certified Service Provider	FISSEQ	Fluorescent In Situ Sequencing	MERFISH	Multiplexed Error-robust Fluorescence In Situ Hybridization	TME	Tumor Microenvironment	NSCLC	Non-Small Cell Lung Cancer
DA	Data Analysis	G / GEJ	Gastric / Gastroesophageal End Junction	MGH	Massachusetts General Hospital	UC	Urothelial Carcinoma	PCNSL	Primary Central Nervous System Lymphoma
DAS	Data Analysis Service	GOG	Gynecologic Oncology Group	IA	Image Analysis	WM	Waldenstrom Macroglobulinemia	PICI	Parker Institute for Cancer Immunotherapy
DL	Deep Learning	HCC	Hepatocellular Carcinoma	IBD	Inflammatory Bowel Disease	WSI	Whole-Slide Imaging	WW	Worldwide

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- Introduction & Methodology
- Executive Summary
- Market Analysis
- Publication Analysis
- Primary Market Research
- Competitive Analysis

DeciBio estimates the worldwide Spatial Biology market is ~$320M in 2022 and is expected to grow at ~30% p.a. to reach ~$1.2B in 2027 (1/2)

Overall Market; Drivers and Moderators

$M

Year			CAGR
	$1,500		
	$1,200M		30%
	$160M		>100%*
	$1,000		
	$730M		
	$360M		24%
	$500		
	$680M		29%
	$0		
	$320M		

2022 2025 2027

■ Routine Clinical Dx ■ Basic Research ■ Translational & Clinical Research

Drivers

Early Validation — Early data reinforces the utility and novel biological insights derived from spatial analyses; the rise in immuno-oncology provides an optimal application for spatial analysis tools

Better Tools — Improvements in the capabilities, ease of access, and flexibility of platforms and chemistries spurs adoption / utilization

Digital Pathology — Advances in analytical capabilities via digital pathology and AI-based image analysis algorithms enable deep insight generation

Industry Excitement — Hype (and funding) for spatial technologies and companies drives interest these novel tools

Moderators

Data Immaturity — Lack of large, prospective, primary outcomes clinical data for spatial signatures disincentivizes adoption in the clinic today

Cost — High cost per assay (e.g., up to $5K per slide), and bioinformatics costs (e.g., up to another $5K per slide or more for multiple analyses)

Scalability Concerns — Though efforts have been made to increase throughput, it is still limited (e.g., ~20 slides / day for a 3-6-plex mIF slide, versus as low as 1 slide / day for 20+ plex)**

Immature Infrastructure — Regulatory and payor policies are not adapted to support high-plex tissue analysis; additionally, adoption of the physical platforms that support such analyses is limited

Moving Forward: spatial biology is expected to see rapid growth; customers across segments express excitement about spatial technologies across all stages of the R&D pipeline; incorporation of spatial into pivotal studies by pharma and anticipated approvals will drive the next wave of growth

Notes: * Excludes multiplex tissue analysis in clinic today (e.g., PIN4, Uro-3 assays) excluded due to primarily non-spatial analysis
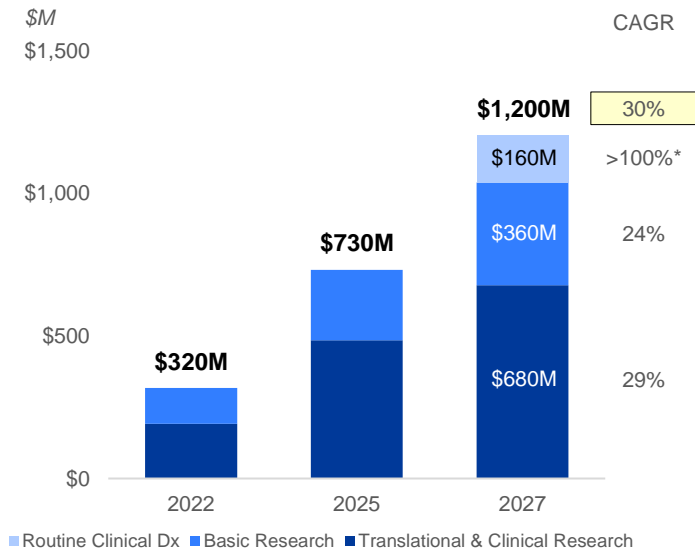   ** Standard BioTools Hyperion+ claims 20 slides / day for 40+ plex proteomic analysis, though this method is somewhat discounted for scalability due to high per assay cost
Source: DeciBio Analysis

DeciBio estimates the worldwide Spatial Biology market is ~$320M in 2022 and is expected to grow at ~30% p.a. to reach ~$1.2B in 2027 (2/2)

Spatial Biology Market Trends

$M

CAGR

- **2022:** $320M
- **2025:** $730M
- **2027:** $1,200M — 30%
  - Routine Clinical Dx: $160M — >100%*
  - Basic Research: $360M — 24%
  - Translational & Clinical Research: $680M — 29%

Chart values:
- $1,500
- $1,000
- $500
- $0

Years: 2022, 2025, 2027

Legend: ■ Routine Clinical Dx ■ Basic Research ■ Translational & Clinical Research

- While initial traction has been strong, especially in basic and translational research, spatial biology is in early stages of adoption today; customers are still evaluating and validating various platforms for broader use
  - Key research applications include:
    - Assessment of the tumor microenvironment, including analysis of the immune cell contexture within a tumor before and/or after treatment with immunotherapy, to understand pathophysiological mechanisms of disease
    - Assessment of tissue inflammation processes across multiple tissue types (e.g., infectious diseases, autoimmune diseases)
    - Single-cell gene expression patterns and cell-type characterization
    - Identification of spatial signatures that can predict response to treatment

- Over the next 5 years, researchers expect to increasingly transition from pilot / exploratory studies to larger scale validation / registrational studies; this will be a key driver of growth
  - Improvements in workflow, cost, and standardization will be needed to support the investment in spatial technologies as a clinical trial and CDx tool

- Diagnostic use is limited today; a CDx approval is expected in 3 – 5 years for a low-plex (e.g., 3 – 6 plex) assay; significant Dx upside remains beyond 2027

Moving Forward: significant market upside is expected beyond the forecast window of this report as spatial signatures gain more traction in the clinic and the clinical infrastructure evolves to support broader adoption of spatial biology Dx globally

Spatial transcriptomics analysis drove the spatial biology market in 2022; mIF and multi-omic approaches are expected to accelerate growth toward 2027

Spatial Biology Market Technologies
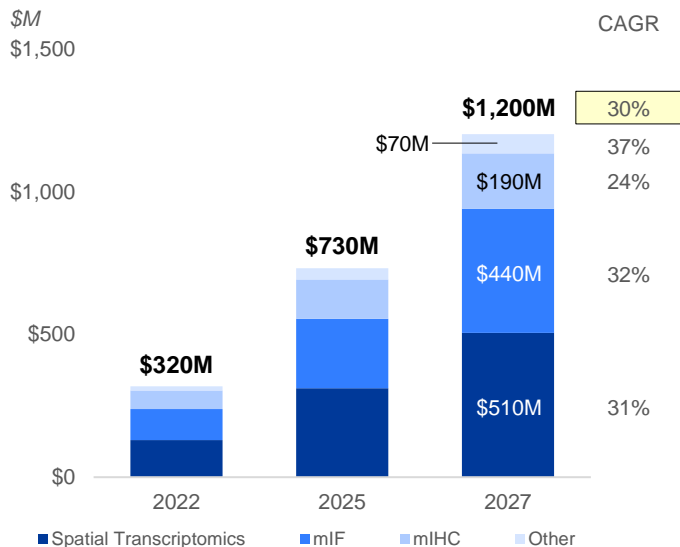
- **Spatial RNA:** spatial transcriptomic platforms enable high-plex (e.g., up to whole transcriptome) discovery research and increase the data per slide
  - o Newer spatial transcriptomic platforms introduce competitive pricing dynamics, though absolute price per slide is expected to remain high
  - o Low-plex RNA-ISH (e.g., 1 – 3 plex) also has relevant spatial clinical / research applications, and is being explored for CDx applications
  - o At single-cell resolution, spatial methods will compete with traditional single-cell methods

- **mIHC/mIF*:** proteomic phenotyping is especially useful in immuno-oncology where cell surface expression dictates immune response and may inform prognosis / Tx response
  - o mIHC / mIF is optimal for smaller signatures of 2 – 8 plex; mIHC is best suited for 2-4 plex, while mIF is optimal for 4 – 8 plex
  - o Initial positive data**, new and more robust platforms, and potential clinical use will likely drive use during the forecasted period
  - o High cost versus traditional (non-spatial) IHC techs may moderate adoption; the lack of a spatial signature for Dx / CDx would be a moderator as well

- **Other Spatial-Omics:** techs such as imaging mass cytometry offer high plex proteomic capabilities and will carve out niches in research segments

Moving Forward: all spatial techs are likely to see expanded use, though increased biopharma utilization of mIF in clinical research (e.g., as they de-plex from high-plex translational signatures to lower-plex clinical signatures) will be one of the key drivers

The spatial biology market is expected to be balanced across key customer types however, utilization will vary; clinical adoption is expected on the ~5 year horizon

WW Spatial Biology Market by Customer* (2022-27)

$M

	CAGR
$1,200M	30%
$70M	>100%
$160M	25%
$320M	31%
$320M	42%
$320M	21%

$730M

$320M

Legend: ■ Academia ■ CRO / Ref Lab ■ Biopharma-Large ■ Biopharma- Small ■ Clinical (Hospitals)

Years: 2022, 2025, 2027
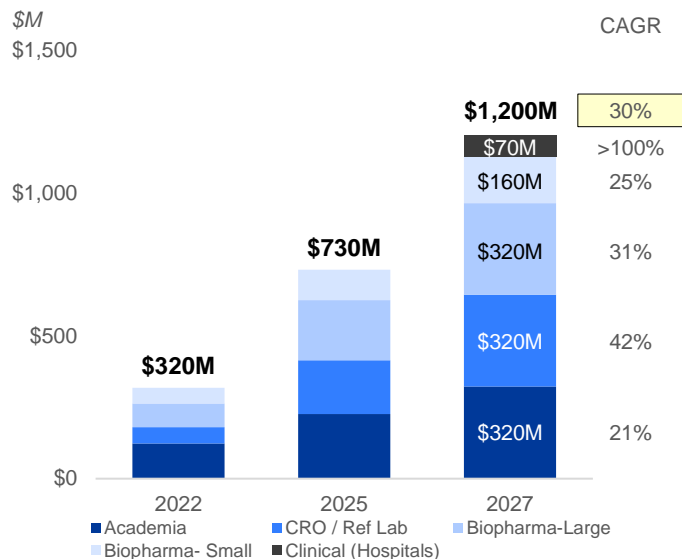
- **Large Biopharma:** expected to maintain high spatial biology market share at ~25% of 2027 spend; they spend significantly on spatial services for transcriptomics and mIF, utilizing these techs primarily for biomarker discovery, response prediction, and prognosis in immuno-oncology

- **Small-Mid Biopharma:** expected to make up ~15% of 2027 spend; while nearly all large biopharma are exploring spatial analysis to some extent, we estimate that ~25% of small biopharma are leveraging spatial analyses in their research and trials

- **Academia:** expected to make up ~25% of 2027 spend; academic customers access spatial technologies through core labs and have driven a significant portion of early spatial research; this early establishment is expected to moderate growth

- **CROs / Ref Labs:** do not regularly initiate their own spatial biology research (<10%) but support much of biopharma spatial testing (>50%); CROs / ref labs are a key market enablers given high CapEx; they are expected to support most clinical testing

- **Hospitals / Clinical:** In-house clinical testing expected to come online in ~2026; these customers are expected to make up ~$70M of the market (~5%) in 2027, most likely for mIHC and mIF assays on fully automated platforms / existing equipment

Moving Forward: As spatial signatures become analytically and clinically validated, and move further into clinical trial pipelines (e.g., registrational studies), CROs are expected to take on increasing volume share; mIF utilized in clinical trials will likely make up a significant portion of this growth

NanoString, Akoya Biosciences, and 10x Genomics are projected to be spatial biology market leaders in 2027, though the market will support multiple players

Spatial Biology Competitor Overview

$M

CAGR

Chart axis values: $1,500 / $1,000 / $500 / $0

$320M (2022)

$730M (2025)

$1,200M — **30%** (2027)
- $370M — 27%
- $260M — 28%
- $570M — 35%

Legend:
- Akoya Biosciences
- NanoString
- 10x Genomics
- Bio-Techne / ACD
- Ultivue
- NeoGenomics
- Standard BioTools
- Ionpath
- Other

AKOYA BIOSCIENCES
Akoya Biosciences has seen rapid growth as a translational research mid-plex mIF provider whose sights are balanced well between the clinical aspirations and discovery research support; expecting spatial revenues of ~$70M for 2022

nanoString
NanoString sees high adoption in academia and biopharma R&D labs for their GeoMx Digital Spatial Profiler; saw spatial revenues of ~$50M in 2021

10x GENOMICS
10x Genomics is expected to capture heavy academic use with 2 spatial RNA platforms (Visium and Xenium); the Visium platform continues to see uptick in adoption with the launch of CytAssist

ACD a bio-techne brand
Advanced Cell Diagnostics (ACD) sees widespread use of the RNAscope platform and has initiated some CDx partnerships; its assays are at a relatively low price point compared to competitors

Ultivue
Ultivue has an open, decentralizable mIF solution; it has made multiple partnerships with imaging and instrument leaders to provide a complete workflow

NEO GENOMICS
NeoGenomics sees heavy large biopharma service usage as a market-leading oncology specialty CRO, and offers both proprietary (MultiOmyx) and third-party offerings

Additional company details included in key player profiles section

Moving Forward: NanoString, Akoya, and 10x Genomics are expected to remain revenue leaders through 2027, though multiple other players will capture share as new platforms are validated; a services-oriented market will enable researchers to explore multiple providers and technologies

Source: DeciBio Analysis

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- **Market Analysis**
- Publication Analysis
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The spatial biology field is burgeoning, with technologies covering multiple analyte types; the space has attracted interest from multiple players

Spatial Biology Field By Analyte – <u>Select</u> Players*

RNA / DNA^	RNA + Protein	Protein

RNA / DNA^: 10x GENOMICS, Acuity Spatial Genomics^, ACD Advanced Cell Diagnostics, Enzo, resolve biosciences, vizgen

RNA + Protein: nanoString, RARECYTE Precision Biology for Life Sciences, REBUS BIOSYSTEMS, Spatial Genomics

Protein: veracyte, abcam, AKOYA BIOSCIENCES, BETHYL A FORTIS LIFE SCIENCES COMPANY, NEO GENOMICS, Canopy BIOSCIENCES, Cell IDx context matters, cytiva, Ultivue Profiling Cancer Biology, Leica MICROSYSTEMS, Lunaphore technologies, MACS Miltenyi Biotec, vector LABORATORIES, Roche, STANDARD BIOTOOLS, SYNCELL, BIOCARE MEDICAL, IONPATH

All-Omic / Services*: AmberGen, BIO SYNTAGMA, CellCarta, CELLECTA, Cerba Research, CROWN BIOSCIENCE, Flagship BIOSCIENCES, indivumed, labcorp Drug Development, Propath From Biology to Data, Q² Solutions, VISIKOL A BICO COMPANY

> Note: the spatial biology market consists of an ecosystem of companies, including those offering imaging / scanning / microscopy equipment as well as those offering image analysis products and services – this report focuses on companies with proprietary multiplex / spatial chemistries or methods, and service providers that offer multiplex / spatial wet-lab services

Notes: * Non-exhaustive; includes companies with proprietary spatial technology planforms / chemistries as well as service providers / CROs offering spatial profiling services; companies included were those that came up most prominently in our secondary and primary research; excludes companies that offer assay components (e.g., antibodies, dyes) but not products packaged and marketed for multiplex or spatial analysis; also excludes companies with primarily image analysis / digital pathology offerings or with primarily imaging / microscopy offerings

Source: DeciBio Analysis

Spatial biology is being implemented in distinct ways across the research and clinical value chain, with lower-plex, simpler assays nearest to the clinic

Use of Spatial Analysis Across the Research and Clinical Value Chain^

	High	Utilization	Low

	Basic Research	Translational Research	Clinical Trials	Clinical Dx
Common Use Cases Today	• Discovery and characterization of biological processes	• Biomarker discovery and validation, for patient prognosis / stratification / treatment selection	• Exploratory outcomes • Patient stratification / therapy selection (e.g., CDx)	• Subtyping / differentiation (e.g., PIN4 for prostate cancer; URO-3 for bladder cancer); though less "spatial" than emerging CDx
Common Analytes / Technologies^	• Spatial transcriptomics • mIF / high-plex proteomics • mIHC	• Spatial transcriptomics • mIF / high-plex proteomics • mIHC	• mIHC • RNA-ISH • mIF	• mIHC
Plex Range	• 2 – 50+ / whole transcriptome; weighted towards higher plex	• 2 – 50+ / whole transcriptome, with the goal to de-plex as much as possible	• 2 - 8 plex	• 2 – 3 plex, expectation for up to 6 plex in the mid term
Trends / Future Outlook*	• Increasing integration of novel multi-omics spatial data (e.g., beyond RNA / proteins) at high plex and single-cell / sub-cellular resolution	• H&E "molecular phenotyping" via image analysis algos. • Integration of spatial histological, genomics, and clinical data • Ongoing outsourcing	• Shift from early-stage / exploratory studies to enrollment / registrational studies • Increasing use of mIF, RNA-ISH • Preference for distributable solutions / kits (offered / operated through CROs)	• Expected approval of low-plex (e.g., 2-4 plex) mIHC, mIF, and / or RNA-ISH CDx tests for I/O • Aided by increasing adoption of digital path • Preference for distributable solutions / kits (with central lab partners)

While spatial biology has most been applied to basic / discovery research applications to-date, there are signs of progress towards clinical utility

Translational / Clinically-Oriented Spatial Research and Commercial Activity*

Translational Studies / Analytical Validation (Select Examples)

AKOYA BIOSCIENCES®

- Study showing mIF spatial signature outperforms TMB and GEP for predicting response to anti-PD1/L1 CPI
- A six-plex mIF panel showed 90% equivalence with IHC across all markers, and high inter- and intra-lab concordance, as is needed for clinical adoption

veracyte

- Study showing that a spatial PD-L1 / CD8 signature) predicts response to neoadjuvant treatment in rectal cancer

Yale NewHaven Health

- Study showing that select expressed genes in distinct tissue compartments can predict survival to ICI

THE UNIVERSITY OF TEXAS MDAnderson Cancer Center Making Cancer History®

- Study showing that B-cell rich tertiary lymphoid structures enrich for responders to pembrolizumab in sarcoma

MOFFITT CANCER CENTER

- Study showing that a classifier trained on the spatial distribution of cell types can predict response to a CPI combination therapy in NSCLC at >90%

Commercial-Clinical Developments

AKOYA BIOSCIENCES® Acrivon Therapeutics

- Akoya Acrivon partnership to develop OncoSignature test as ACR-368 CDx

AKOYA BIOSCIENCES®

- Akoya secures CLIA lab certification for its spatial biology assays to serve pharma trials

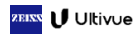**AKOYA BIOSCIENCES® AstraZeneca**

- Akoya partners with AstraZeneca to develop predictive spatial assays for clinical trials

Roche PathAI

- Roche, BMS, and PathAI partner on a spatial CD8 biomarker assay and algorithm

Lunaphore technologies

- Massachusetts General Hospital partners with Lunaphore to develop spatial diagnostics to predict response to PARPi

ZEISS U Ultivue

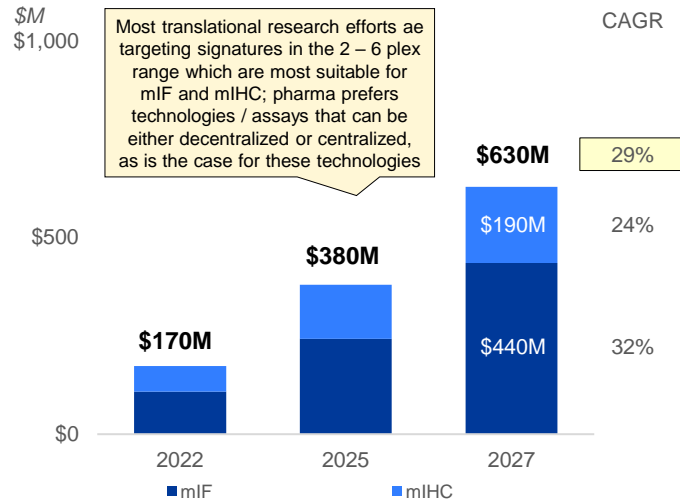- Ultivue partners with Zeiss to co-market complete solution for spatial phenomics with clinical aims

mIHC / mIF is poised to see continued clinical research use; the increase in robustness of mIF platforms supports the movement toward an early spatial CDx

WW mIHC / mIF Market (2022-27)*

$M

Most translational research efforts ae targeting signatures in the 2 – 6 plex range which are most suitable for mIF and mIHC; pharma prefers technologies / assays that can be either decentralized or centralized, as is the case for these technologies

CAGR

$1,000

$630M   29%

$500

$380M $190M   24%

$170M $440M   32%

$0

2022   2025   2027

■ mIF   ■ mIHC

"…As we move closer to the clinic, reducing the panel size to fit on a more manageable and robust tech, like mIHC or mIF, will be necessary…"

- Executive Director, Translational Research, Large Biopharma

Forecast	Drivers	Moderators	Trends

~29% growth — The mIHC / mIF market is expected to grow ~29% p.a., from ~$170M to ~$650M in 2027, with mIF accounting for the majority of growth

Clinical Infrastructure — mIHC and mIF leverages more standard lab equipment and workflows than higher-plex approaches, making it more accessible, even in the clinic

Increased Automation — An increase in the robustness of products and systems which automate staining and imaging processes lowers the barrier of entry for users

Nascent Clinical Utility — Though initial data is positive, spatial signatures are not commonly used in prospective late-stage trials with registrational potential today; additionally, some spatial profiles can be reduced to bulk gene expression signatures, which are simpler to implement clinically

Cost — Cost for multiplex spatial assays is usually higher than running multiple single-plex assays to cover the same markers; reimbursement for multiplex diagnostics is unfavorable

De-Plexing — De-plexing of signatures identified from high-plex analyses into the few biomarkers that drive the meaningful signal so that it can be adapted to mIHC or mIF and existing instrumentation

DigPath Enablement — mIF players are making efforts to partner with leading digital pathology providers to gain the most insight from multiplex assays

Notes: * Other bucket consists of IMC, GeoMx proteomics extension, and other technologies, and is valued at <$100M to grow at similar market rates but is not detailed in this section
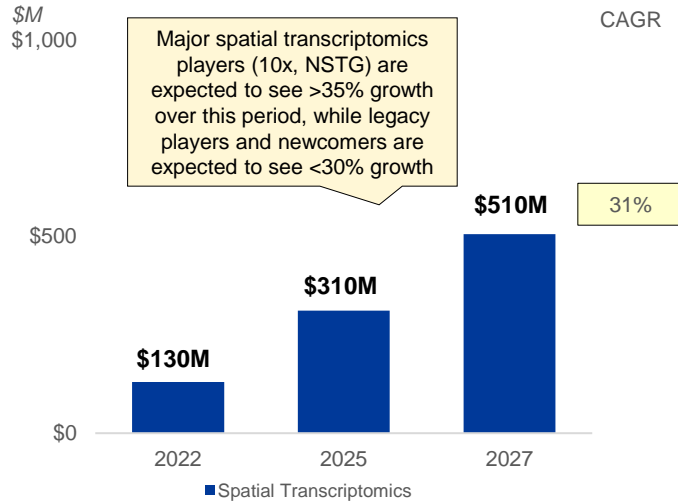Source: DeciBio Analysis

24

Spatial transcriptomics is used in academia and biopharma discovery today, though cost and data analysis barriers limits scaling to high-volume applications

WW Spatial Transcriptomics Market (2022-27)

$M

CAGR

Major spatial transcriptomics players (10x, NSTG) are expected to see >35% growth over this period, while legacy players and newcomers are expected to see <30% growth

$1,000

$510M — 31%

$500

$310M

$130M

$0

2022 · 2025 · 2027

■ Spatial Transcriptomics

"…Sure, [spatial transcriptomics] is a more expensive platform, but the amount of data we get from a few samples can fuel months of investigation…"

- Executive Director, Translational Research, Large Biopharma

Forecast	Drivers	Moderators	Trends

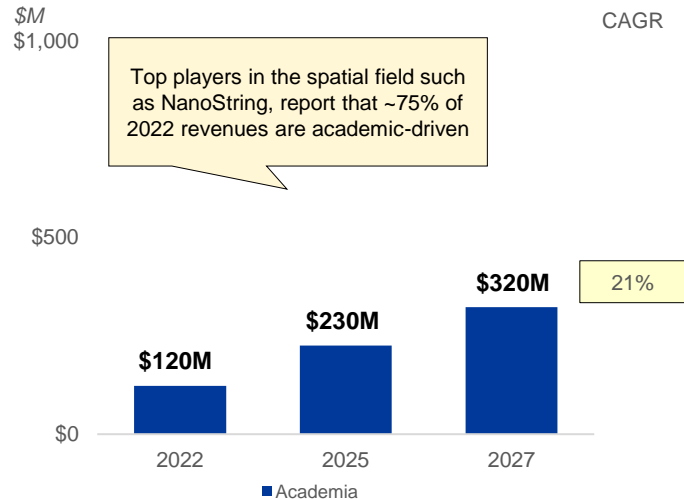|	
~31% growth	Spatial transcriptomics market is expected to grow ~31% p.a., from ~$130M to ~$510M in 2027
scRNA Market Conversion	As spatial technologies achieve single-cell resolution, they are expected to capture share from the established traditional single-cell omics market
RNA-ISH Performance	RNA-ISH is as sensitive, if not more so, than IHC, and can be run on standard clinical pathology equipment; it is robust and validated for Dx use
Bioinformatics Improvements	Commercially-available / open-source bioinformatics solutions are increasingly accessible and improving, facilitating complex data analysis
High Cost	Capital and per-sample costs are often high (e.g., up to ~$4K / slide), with substantial analytical costs as well, limiting use to small projects
Difficult Data Analysis	Despite improvements, the analytical burden and time requirement (for high-plex analyses) is too high for routine clinical use
Workflow Complexity	Assay protocols are not analytically validated for Dx use; additionally, throughput is too low for Dx use
Spatial Multiomics	Utilization of multi-omic solutions which include both proteomic and transcriptomic markers, largely in preset panels, is emerging
Increased Competition	NanoString will see spatial transcriptomic instrument competition from 10x Genomics with the launch of the CytAssist and Xenium platforms

25

Growth in academia will be driven by broad core lab adoption, new technologies, and higher utilization as data analysis improves; cost remains prohibitive

WW Academic Spatial Market (2022-27)

$M

Top players in the spatial field such as NanoString, report that ~75% of 2022 revenues are academic-driven

CAGR

$1,000

$500

$120M (2022)

$230M (2025)

$320M (2027)

21%

$0

■ Academia

"…[Spatial Biology] is inherently an enabling tech class. We're asking entirely new questions…"

- PI, Academia

Forecast	Drivers	Moderators	Trends

~21% growth	The established academic spatial biology market is expected to grow ~21% p.a., from ~$120M to ~$320M in 2027
Bioinformatics Enablement	Better data analysis enables researchers to ask more questions and explore more hypotheses, and decreases analysis time, allowing researchers to analyze more samples
Novel Capabilities	New platforms with novel capabilities (e.g., increasing resolution, novel analytes, multi-omics capabilities) will enable exploration of new hypotheses
Cost	Higher plex methodologies often increase cost significantly; high CapEx and service prices limit the scale of experiments and adoption
Complex Analysis	Data analysis capabilities seem to be lagging the rate of advancement in plex, resolution, and multi-omics data generation
Non-Oncology Use	Increasing recognition of spatial-omic value in non-oncology therapeutic areas (e.g., neuroscience, infectious disease) increases the breadth of applications
Multi-Omics	Increased adoption of spatial technology with proteomic sub-analyses or combined transcriptomic-proteomic analyses
Outsourcing Image Analysis	As the technology improves / evolves, image analysis requirements are exceeding internal capabilities of researchers, driving reliance on 3rd-party image analysis companies; AI is becoming a common need

Notes: *
Source: DeciBio Analysis

Biopharma is positioned to drive high growth in spatial biology use, however widespread and long-term adoption hinges on demonstration of clinical utility

WW Biopharma Spatial Market (2022-27)*

Forecast   Drivers   Moderators   Trends

Current reimbursement structure is unfavorable toward multiplex assays; changes in reimbursement incentives will be required to convince pharma that multiplex CDx tests can achieve traction in clinical testing

$M
$1,000

$500

$480M   29%
$160M   25%
$320M
$320M   31%
$140M

$0
2022   2025   2027

CAGR

■Biopharma-Large   ■Biopharma-Small
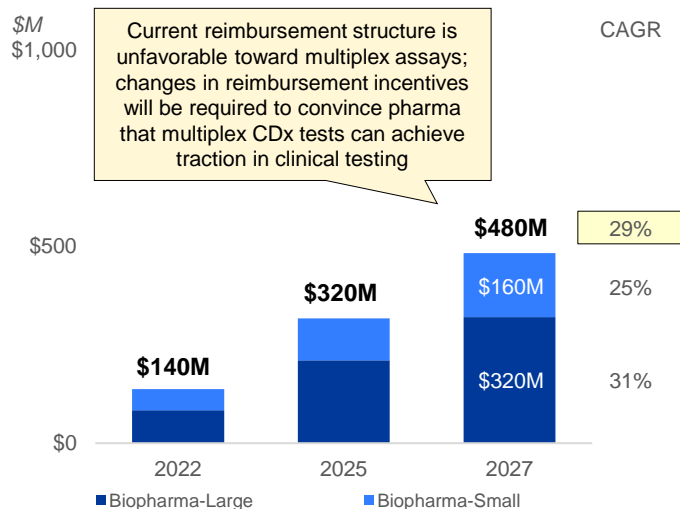
"…The past couple years have been focused on turning these small-scale retrospective insights to larger-scale prospective studies…"

- Head, Oncology Translational Research, Large Biopharma

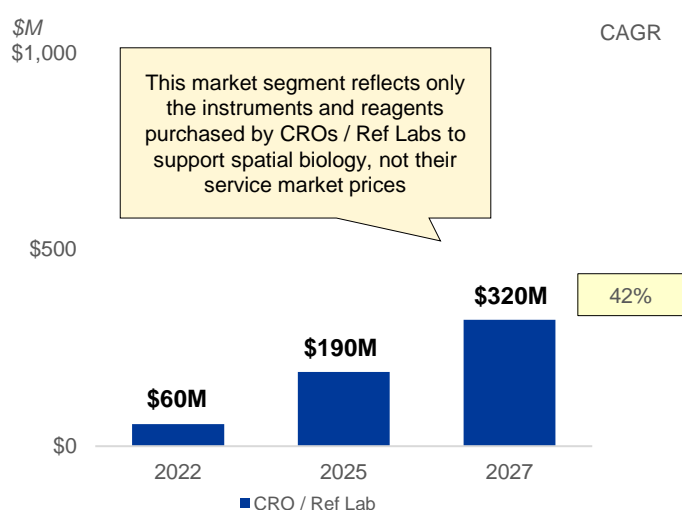|	
~29% growth	Biopharma will use more spatial analysis in translational / clinical work, and is expected to grow ~29% p.a., from $140M to reach ~$480M in 2027
CLIA-grade CROs	CROs / ref. labs offering spatial are maturing clinically (e.g., gaining CLIA accreditation, validating assays), enabling them to support registrational trials
Initial Positive Data	Richness of initial spatial biology data and signals of clinical utility have increased interest in the field and encourage more use of the technology**
Evolving Treatments	Emerging analyte classes and combinations (e.g., checkpoint inhibitors, PARPi, bi-specifics, cell therapies, etc.) drive the need to understand complex processes; additionally, a shift of precision medicine to earlier lines provides access to optimal tissue samples (e.g., resected tumor, rather than biopsies)
Lack of Scalability	Cost and throughput limitations can moderate the number of patients from which spatial data is collected; costs are perceived as too high to be used across all patients in a registrational study
Regulatory Uncertainty	Validation requirements for a spatial signature are unknown, incentivizing pharma to translate signals to validated methods (e.g., GEP) when possible
Integration w/ Genomics	Many pharma have banked samples containing comprehensive genomic and clinical data, integration of spatial biomarker data significantly scales the analytical space
Translating to Lower Plex	As research advances toward later translational stage, pharma will continue to favor lower-cost lower-plex methods (e.g., mIHC, RNA-ISH, mIF)
Increased Service Use	Across all stages of research and development, reliance on service providers is expected to be high, especially as multiplex / spatial signatures gain more traction in prospective clinical trials

Notes: * Includes both spend on instruments and reagents for in-house research as well as spend on services paid to CROs / ref labs; ** Additional detail on initial positive data given on slide 22
Source: DeciBio Analysis

Due to the rapidly-evolving pace of advancement, increasingly complex analyses, and increasing use in prospective studies, the role of service providers will grow

WW CRO / Ref Lab Spatial Market (2022-27)*

Use Case	Drivers	Moderators	Trends

$M
$1,000

CAGR

This market segment reflects only the instruments and reagents purchased by CROs / Ref Labs to support spatial biology, not their service market prices

$500

$320M — 42%

$190M

$60M

$0

2022   2025   2027

■ CRO / Ref Lab

"…We're seeing large biopharma come in as repeat customers with larger and larger spatial projects. It's only a matter of time before we see clinical scaling…"

- CEO, Specialty Spatial CRO

~42%	CROs / Ref Labs are tooling-up to support maturing pharma research, growing ~42% p.a., from ~$60M to ~$320M in 2027
Differentiating Expertise	Expertise in spatial technology can be used to differentiate service offerings from generic CRO competitors
Standard-ization	Centralization of analysis provides more consistent, standardized, reproducible data from complex workflows, both for research and ultimate clinical Dx use
Clinical Utility / CDx	Clinical validation of a spatial CDx signature is expected within the forecast window, most volumes for such a test are likely to be centralized
Geographic Reach	Specialty CROs / Ref Labs are less established globally and may lack access to international markets needed to support global trials
Lack of Scalability	As use of spatial matures and the size of studies increase, throughput may become an issue for specialty labs; few have the scale and quality systems in place to support registrational studies or clinical testing
Partnership Ecosystems	Spatial platform / chemistry developers, CROs, and imaging providers are partnering to provide best-in-class, streamlined workflows
One-Stop-Shop-ification	CROs are adopting multiple types of spatial platforms (e.g., proteomics, transcriptomics, low-mid plex, high plex) to support pharma as they continue to explore various modalities

Notes: * Includes spend on spatial biology instruments and reagents; does not include revenues generated by the provision of services
Source: DeciBio Analysis

Spatial biology is expected to remain primarily a translational research tool for the near-mid term, and see initial traction in the clinic within 5 years

WW Spatial Biology Market by Application (2022-27)

Market Forecast

Discovery
$M
$1,000
$500
$0

$130M (2022), $250M (2025), $360M (2027)

Basic Research is expected to grow 24% p.a., from $130M to $360M in 2027

- Higher resolution and plex platforms, as well as integrated spatial multiomics, will enable researchers to ask more and more detailed questions
- As researchers become more familiar with the spatial tools, and data analytics, they are likely to increasingly expand use outside of oncology studies
- Rate of growth will be highly tied to platform adoption by core labs, which do not turn-over instruments quickly and require grants for new ones

Translational
$1,000
$500
$0

$190M (2022), $480M (2025), $680M (2027)

Translational/Clinical Research is expected to grow 29% p.a., from $180M to $680M in 2027

- Pharma is continuously seeking to extract as much information as possible out of clinical trial samples, and using spatial analysis to do so; spend / attention will shift to larger, more strategic studies
- Spatial technologies may compete with other analytical modalities for trans. research budget – e.g., some pharma is exploring whether tissue phenotyping can be achieved using novel liquid biopsy analyses
- Various "label-free" spatial analysis methods are emerging (e.g., that leverage H&E or auto-fluorescence w/ dig. path. to generate spatial algos)

Routine Clinical
$1,000
$500
$0

Excluding current clinical multiplex analyses* due to lack of spatial content of output

$0M (2022), $0M (2025), $160M (2027)

Routine Clinical Dx is expected to reach $160M by 2027

- Despite promising translational data, both technological and commercial barriers exist to implementation of spatial biology Dx in the clinic
  - Cost, workflow, throughput, standardization are all sub-optimal for routine Dx use
- Select players (e.g., Akoya, ACD) have established early-stage CDx partnerships; success is TBD
- Due to the immaturity of the commercial infrastructure, spatial Dx / CDx is likely to require centralization to a reference lab
- Ultimately, stakeholders don't care about spatial vs. non-spatial biomarkers, clinical utility will drive regulatory, payor, and clinical acceptance

29

Use of plex varies by research stage; basic and discovery research utilize high-plex panels, while plex decreases along the clinical trial pipeline

WW Spatial Biology Market by Plex (2022-27)

> Market share not reflective of volume share due to significant price discrepancies between low- and high-plex tests and reliance on services (vs. kits) for the latter

Market Forecast

2-3 Plex*
$M $1,000

$500

- 2022: $40M
- 2025: $110M
- 2027: $240M

2-3 plex is expected to grow 41% p.a., from $40M to $240M in '27

- Low-cost and relatively high throughput, largely mIHC; can often leverage existing lab equipment
- Pharma will prefer to deplex any CDx as low as possible
- Often used today for analysis of 1-2 types of TILs or TILs + a therapeutic marker of interest
- Still requires use of digital pathology for most analyses

4-8 Plex
$1,000

$500

- 2022: $80M
- 2025: $190M
- 2027: $290M

4-8 plex is expected to grow 28% p.a., from $80M to $290M in '27

- Plex range largely supported by mIF technology, though some mIHC techs can address this range
- Workflow complexity increases moderately – often requires cycling or multiple slides, however, kitted solutions available for decentralized use
- Likely to represent the majority of translational volumes, and potentially some clinical testing as well

9-20 Plex
$1,000

$500

- 2022: $70M
- 2025: $150M
- 2027: $220M

9-20 plex is expected to grow 25% p.a., from $70M to $220M in '27

- Plex achievable via mIF (but with mixed results), spatial transcriptomics, or IMC more common
- Both CapEx and per-sample costs increase significantly at this level; majority of analysis >9 plex will be outsourced to core labs and/or CROs
- Varying levels of spatial resolution available
- Highly complex bioinformatics

20+ Plex
$1,000

$500

- 2022: $120M
- 2025: $280M
- 2027: $450M

20+ plex is expected to grow 31% p.a., from $120M to $450M in '27

- Supported by IMC and spatial transcriptomics, various novel methods offered, no gold standard
- Highest cost per slide (e.g., up to $10k+ for wet lab + analysis services)
- Primarily used for exploratory / discovery research to identify a smaller subset of markers of interest
- Highly complex bioinformatics

Notes: * Due to the low relative cost of 2-3 plex assays, the volume share of the 2-3 plex assay market is significantly higher than the $ value; does not include assays without spatial readouts
Source: DeciBio Analysis

The U.S. is expected to remain the market leader through 2027; research applications are expected to be similar globally, though clinical Dx dynamics would differ

WW Spatial Biology Market by Geography (2022-27)

Recently, global supply chain disruption, foreign exchange pressures, and macroeconomic headwinds have weighed on ex-U.S. revenues of U.S. manufacturers of spatial products – this may persist in the near term

Market Forecast

$M

U.S. (flag)
- $1,500
- $1,000
- $500
- $0
- 2022: $180M
- 2025: $370M
- 2027: $600M

The U.S. is expected to grow 27% p.a., from $180M in '22 to $600M in '27

E.U. (flag)
- $1,500
- $1,000
- $500
- $0
- 2022: $70M
- 2025: $190M
- 2027: $310M

The E.U. is expected to grow 33% p.a., from $70M in '22 to $310M in '27

ROW (globe)
- $1,500
- $1,000
- $500
- $0
- 2022: $60M
- 2025: $170M
- 2027: $290M

The ROW is expected to grow 35% p.a., from $60M in '22 to $290M in '27

- The majority of spatial biology instrument / assay manufactures and service providers are U.S.-based
- Large number of academic medical centers will drive basic and translational research
- Existing centralized reference lab testing infrastructure and regulatory pathways (e.g., single-site PMA) are amenable to the incorporation of complex tests into clinical care
- Willingness to adopt and pay for premium biomarker / diagnostic solutions is higher than in the EU or ROW

- Similar to the U.S., spatial biology research is likely concentrated in academic centers (core labs) and pharma; investment in innovation remains high*
- Lack of a robust centralized laboratory infrastructure may favor technologies that can be more readily decentralized (at least to key academic labs) – e.g., mIF, mIHC, RNA-ISH
- Generally more advanced adoption of digital pathology in the clinical setting than the U.S., reducing one of the barriers to clinical use; however, coverage of novel Dx tests generally trails the U.S.

- Growing access to precision therapies, including immunotherapies, will drive growing interest in the tumor microenvironment among local research institutions
- Adoption by pharma and AMCs / large research hospitals in China and Japan expected to drive ROW growth
- May favor mIHC and mIF, which can be adopted in-house more readily, due to restricted access to U.S.- and EU-centric CROs and, in some cases, barriers sending samples across borders

Notes: * Funding programs such as German TRR 305 or the EU Horizon Europe funding program contain language regarding support for innovative diagnostic technologies
Source: DeciBio Analysis

31

Agenda

- Introduction & Methodology
- Executive Summary
- Market Analysis
- **Publication Analysis**
- Primary Market Research
- Competitive Analysis

Spatial biology research has been growing steadily, driven by the launch of novel platforms as well immunotherapies, which drive research interest in the TME*

Annual Spatial Biology Publications** (2017-2022)

Spatial Transciptomics was recognized as Nature Methods' *Method of the Year* in 2020

Legend:
- ACD
- Akoya Biosciences
- Nanostring
- 10x Genomics
- Fluidigm
- Other**
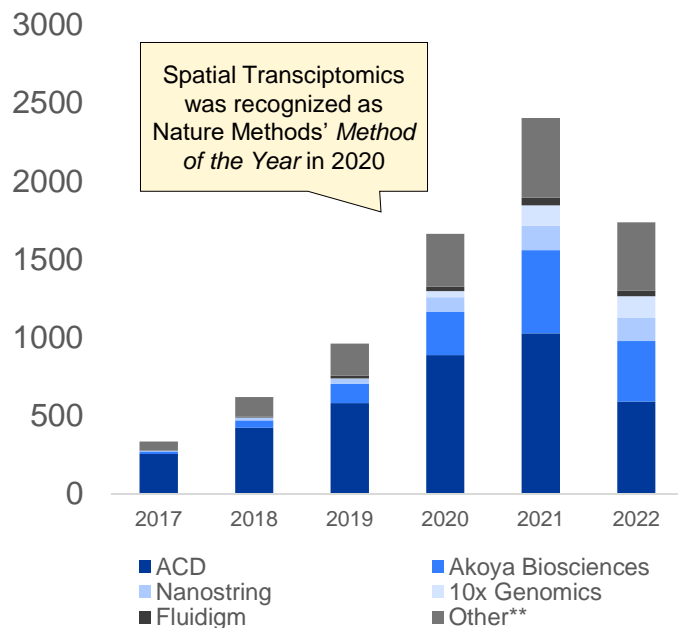
- Fast growth through the past five years, including the period of general economic downtrend during COVID; 2022 YTD is on pace to continue growth at or above 2021 growth rate

- **Akoya Biosciences** saw the highest growth through this time period, fueled by new product launches, high-profile partnerships with large biopharmaceutical players, and consistent marketing
  - Akoya acquired the PerkinElmer Phenoptics brand in 2018, one of the legacy mIF brands with a strong track record of adoption

- **Advanced Cell Diagnostics (ACD)** maintains top publication share with RNAScope, though many of its publications are in the low / single-plex space; RNAScope may also see an additional bump in activity due to inclusion in Akoya panels

- **10x Genomics** and **NanoString** platforms are newer (e.g., both NanoString's DSP and 10X's Visium platforms were launched in 2019), and the pace of publication has quickly ramped since then

- New entrants continue to expand their publication counts by offering novel technologies differentiated by higher plex capabilities; this fragmentation is expected to continue, though consolidation may occur during this time period

Immuno-oncology continues to drive spatial biology forward, though emerging therapeutic areas also show increased market share

Field-of-Study Driving Publications (2017-2022)
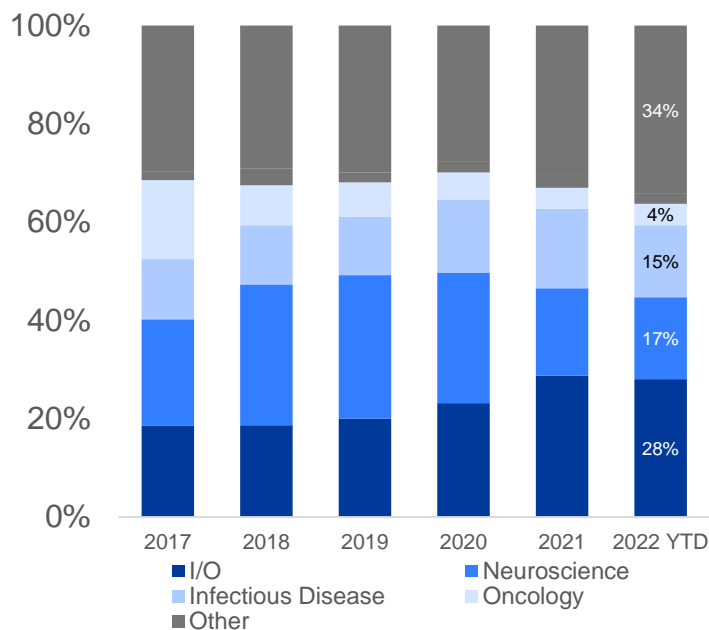
- **Immuno-oncology**: top therapeutic area in 2022, driven by interest in identifying markers in the tumor microenvironment that can predict response to immune checkpoint blockade

- **Neuroscience**: though total publication share has tapered, neuroscience is still a significant portion of the publications due to the inherent need to tracking spatial context in neurological diseases**

- **Infectious Disease**: moderate increase in publication share since 2019 due primarily to COVID-19 research

- **Oncology**: non-immunotherapy oncology has seen a declining share of spatial publications, potentially due to the adoption of non-spatial molecular methods

- **Other**: therapeutic areas outside of those above have increased and are expected to continue to grow as manufacturers and researchers continue explore novel areas

Recent research and commercial activity illustrates the active investment and progress in moving spatial biology closer to the clinic

Top 2022 YTD Activity – **Top 5 Pharma**[1] (1/2)

Key: Product Launch · Trial Launch · Partnership · Clinical Data · Other

	Company	Development	Industry Partners	Indication / Geography	Summary / Implications
(Partnership)	Bristol Myers Squibb / Roche	Roche / BMS collaboration to deploy AI-based DP solutions into clinical trials	PathAI	Not Specified	o **Collaboration to advance 2 DP assays for prospective use in clinical trials** via Roche's NAVIFY platform: (1) pathologist support for the on-market VENTANA PD-L1 (SP142) assay and (**2) a spatial CD8 algorithm developed by PathAI**
(Clinical Data)	3DMed	**AACR 2022 - 6176** - CD56 dim+ immune infiltration and reprogrammed TME[2] associated with response to neoadj. anti-PD-1 + chemo in G/GEJC	N/A	G/GEJC	o **Prospective** 10-plex mIHC for TME evaluation in G/GEJC patients treated with Sintilimab in a Ph 4 SHARED trial (ChiCTR1900024428) o **Several predictors of Tx response to anti-PD-1 identified**
(Clinical Data)	AstraZeneca	**AACR 2022 - 1235 / 7** - Presence of TLS[3] and combined high densities of PD-L1+ macrophages & CD8+ T cells predict OS[4] for Durvalumab-treated NSCLC	N/A	NSCLC	o Computational IA[5] following IHC & 6-plex mIF to identify OS drivers in Durvalumab-treated NSCLC patients in a Ph 1|2 AZ trial (NCT01693562) o **Several multi-parametric drivers of long-term OS identified**
(Clinical Data)	Bristol Myers Squibb	**AACR 2022 - 5222** - Biomarkers associated with CMR[6] to Nivo[7] + BV[8] for treatment of CAYA[9] with R/R cHL in the CheckMate 744 study	Seagen	cHL[10]	o Retrospective mIHC for predictive biomarker analysis of cHL patients treated with Nivo+BV in a Ph 2 BMS trial (NCT02927769) o **CD163+ CD68+ TAMs[11] in the** baseline **TME[2] were associated with CMR**

Recent research and commercial activity illustrates the active investment and progress in moving spatial biology closer to the clinic

Top 2022 YTD Activity – **Top 5 Pharma**[1] (2/2)

Key: Product Launch | Trial Launch | Partnership | Clinical Data | Other

	Company	Development	Industry Partners	Indication / Geography	Summary / Implications
	Roche	**ASCO 2022 - 2626** - Automated tumor immunophenotyping and response to immunotherapy in NSCLC using a spatial statistics approach	N/A	NSCLC	o **Automated predictive biomarker:** AI-based classifier, LATIS[2], to stratify TME[3] into 3 classes[4] w/ different PFS / OS following Atezo^ o Developed / validated on samples from 2 Atezo[5] trials in NSCLC: POPLAR (NCT01903993, Ph 2) and OAK (NCT02008227, Ph 3)
	MERCK	**NCT05281003** - Pembrolizumab Plus Chemo in Neoadjuvant Treatment of ESCC[5]	N/A	ESCC	o **Prospective** mIHC in Ph 2 Merck-sponsored trial of neoadjuvant Pembrolizumab + Chemo in ESCC[5] o **Exploratory endpoint to study mechanisms of Tx response / resistance**
	MERCK	**ASCO 2022 - e18033** - Ph 1/2 study of Pepinemab, an inhibitor of Semaphorin 4D, in combination with Pembrolizumab as first-line treatment of HNSCC	VACCINEX	HNSCC	o Retrospective mIHC to evaluate the TME in an early-stage trial of Pepinemab + Pembrolizumab in HNSCC (KEYNOTE-B84, NCT04815720) o **Ongoing trial, response correlation analysis planned**
	AstraZeneca	**ASCO 2022 - 2596** - Identification of super-exhausted T cells: A novel population predictive of response to immunotherapy	N/A	AST	o Retrospective mIF profiling of ASTs treated with anti-PD1/PD-L1 ICIs[6] as part of an institutional molecular profiling program (NCT02534649) o **Presence of super-exhausted T cells identified as a new predictive biomarker of response to ICIs**

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Customers across all segments expect to roughly double the number of spatial projects and annual spend over the next 5 years

Stakeholder Feedback on Utilization of Spatial Biology

	Estimated # of Samples per Project*		Primary Feedback (select, representative quotes)
	2022	2027	
Academia	3-15	5-20	*"… I could see our use of spatial technology increasing to be 5 times greater than what we currently use. However, our use will depend on if we are getting the biological insights that justify routinely using the assays. Is the spatial context as important as the field thinks it is?…"* - Principal Investigator, AMC, U.S.
Pharma	5-15	10-30	*"… In our Phase 1 studies, it's hard to cover everything we want to. But once we move into Phase 2 trials, we will increase our spend on spatial technology by 3-8x what we currently spend. We'll be moving from 10 - 20 patients per trial, to over 100 patients …"* - Head of Immunology, Small Pharma, Finland *"… If spatial technology shows a benefit, I could see us increasing our use by 30-50% in the next 5 years. But it could also go down by 30-50% if there is no benefit to using it. Right now, the use of spatial is a fishing expedition, with no clear trend for better or worse. We will need to continue to fish for a while until we have more data…"* - Executive Director of Translational Medicine, Large Pharma, U.S.
CROs	20-150	30-500	*"… There's been a reasonable amount of adoption within CROs because of the wealth of information you can get out of the analysis. We're still at the point where we're sorting through to see what's relevant, but I can see growth exploding in the next 5 years…"* - Scientific Director, CRO, U.S.

For academia, cost and data analysis remain key barriers to broader utilization (despite noted improvements in the latter)

Stakeholder Feedback on Current Pain Points in Academia

Academia Key Pain Points	Academia Primary Feedback
Cost • Instrument and reagent cost is prohibitive for many labs, limiting the size of experiments and frequency of use • Service offerings increase cost significantly, depending on the ancillary QC and analysis offered on the front and back end of spatial biology workflows	*"… The entry cost to buy a machine and run samples is very high compared to other technology, like single-cell sequencing. These instruments are primarily placed within shared core facilities because individual labs don't have the budget necessary to buy and maintain the instruments, in addition to the high cost of reagents…"* - Director, Core Pathology Lab, Academia, U.S.
Data Analysis • Complexity of analyses increases significantly versus non-spatial methods, often requiring additional staff or software • Length of time required for analysis increases significantly and can delay deliverables, or change rhythm of publication	*"… Data interpretation is a complex process. In order to do it, you need a bioinformatician and that in and of itself is limiting because bioinformatics is an exploding field…"* - Core Laboratory Pathologist, AMC, U.S.
Ease of Use • Significant expertise is required throughout workflow which may take months or years to acquire • Steepness of the learning curve may deter some from bringing spatial in-house, incentivizing centralization of these tools	*"… Many of my collaborators are hesitant to use this technology because it is not user-friendly. There is a lot of optimization required for each experiment and once the tissue is placed on the slide, there is no way of knowing if the experiment is working until you receive the final results…"* - Computational Biologist, AMC, Canada

Increasing Intensity of Pain Point

Validation and technology standardization are key unmet needs for Pharma and CROs; TAT and scalability also need to improve to support clinical trials and Dx

Stakeholder Feedback on Current Pain Points across Pharma / CROs

Increasing Intensity of Pain Point

	Pharma / CRO Key Pain Points	Pharma / CRO Primary Feedback*
Validation	• Need for both proof-of-concept data showing analytical validation (sens. and spec.), as well as longitudinal data showing predictive / prognostic superiority over other technologies	"… *Platform validation is a key issue that needs to be addressed. Spatial providers need to work with pharma and biotech companies to develop technology that can analyze samples in real-time and to produce prospective data sets*…" - Translational Oncology Lead, Large Pharma, U.S.
Standardization	• Standardization across the entire workflow (i.e. staining, image capture, data analysis) is needed; The burden to develop standardized workflows is on the spatial vendors	"… *The changes you can apply to slides during image analysis can completely change the resulting data. There is currently no standardized way to perform image analysis- everyone uses different methods and algorithms. We need to have general policies and guidelines*…" - Head of Immunology, Small Pharma, Finland
Scalability	• Current TAT is longer than ideal for key pharma applications (i.e., patient enrollment in clinical trials) • Current throughput is too low to support routine use in clinical trials; lack of automation and high hands-on time for initial QC, ROI selection are top bottlenecks currently	"… *Oncologists need to be able to get to the right decision at the right time. They need technology that can help them assign or change therapeutic dosing in time. There are critical timepoints throughout a patient's journey, beginning from sample collection, and we always need to get the results faster*…" - Scientific Director, Small Pharma, U.S. "… *I would like to see an end-to-end approach. For routine use, the technology needs to be scalable and produce accurate data. Automation in the process would be helpful*…" - Scientific Director, Small Pharma, U.S.

Across stakeholder groups, ideal spatial solutions would include improved customizability, automation, and data analysis

Stakeholder Feedback on Ideal Spatial Offerings

	Academia	Pharma	CROs
Instruments / Assays	• A selection of validated pre-built panels, with the ability to customize as necessary "… *I would like to see an 80/20 split, where 80% of the panels are validated, with standard backbone measurements, and the remaining 20% of panels can be customized for individual experiments…*" - Instructor, AMC, U.S.	• A validated platform that allows investigation of broader hypotheses "… *A lot of the assays aren't capturing the biology effectively… we're setting up panels based on a set of a priori hypotheses and not able to go into experiments truly agnostically…*" - Senior Director, Clinical Biomarker Innovation & Development, Large Pharma, U.S.	• A turnkey solution with a fully integrated / automated workflow from sample prep to insights "… *The product offering that will succeed in any of these spaces will be one that allows you to stain, image and analyze all in one instrument- this is true regardless of what stage of research you are in…*" - VP Molecular Diagnostics, CRO
Software	• A combination of integrated analysis solutions and third-party services "… *For simple questions, integrated analysis software will be fine. For more sophisticated experiments, there is a huge space for third-party companies to form and provide complex analysis on a contract basis…*" - P.I., AMC, U.K.	• The analytics software should be offered along with the database for storage "… *Everyone is focused on improving the instrument and the resolution of their offering. If a vendor could develop the analysis software and offer it along with the database component, it would be a huge differentiator…*" - Director of Precision Oncology, Large Pharma, U.S.	• Software that enables the user to perform analysis independently of a third-party "… *Vendors that focus on the analysis portion are in a position to win because many systems that currently offer on-board analysis software leave the customer needing additional help…*" - VP Molecular Diagnostics, CRO

The combination of spatial proteomics and transcriptomics, along with increased resolution at the single-cell level, will define the next wave of spatial biology

Stakeholder Feedback on Future Spatial Advancements

Spatial Proteomics and Transcriptomics	Increased Resolution

"… An offering that combines spatial transcriptomics with proteomics is the future of the spatial biology field…"

- Pathologist, AMC, U.S.

"… At one point, we will need to combine proteomics with transcriptomics for a clinical diagnostic assay, but this is currently a very big challenge…"

- Scientific Director, Small Biotech, U.S.

"… It's no longer sufficient to describe heterogeneity in the transcriptome alone- we need to move beyond the genome and incorporate the proteome as well…"

- PI, AMC, U.K.

"… The ability to profile the transcriptome and proteome in 2D at the same time would be huge. RNA expression doesn't always correspond to protein expression and this would give us the insights we need into cell behavior…"

- Professor, AMC, U.S.

"… If we can truly have single-cell RNA and protein on the same slide, that would be transforming. Thinking past that is difficult…"

- Director of Precision Oncology, Large Pharma, U.S.

"… If companies can provide single-cell resolution, we would have a large shift in spending. We would no longer need transcriptomics- it would be a game changer…"

- Computational Biologist, AMC, Canada

"… I currently don't see any innovation in this space, but high-resolution imaging, on the order of 40x magnification, would advance the field…"

- VP, Molecular Diagnostics, CRO

"… Currently, you can get information on thousands of genes, but you can't say if they are expressed by one cell or another. Companies are beginning to address this by developing platforms with single-cell resolution…"
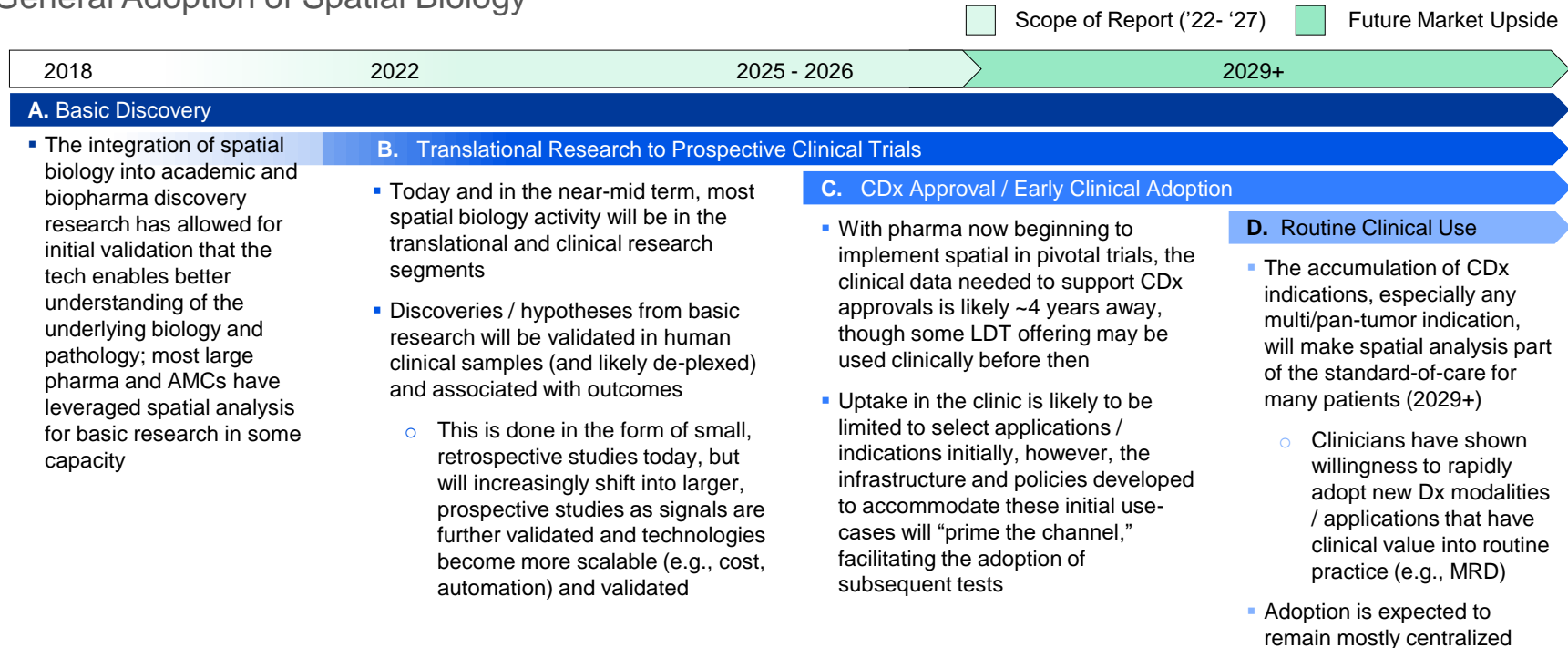
- Associate Professor, AMC, Italy

Experts expect that he first spatial Dx test will likely be a 4 - 8 plex mIF / mIHC assay for use in immuno-oncology; such tests are actively being explored

Stakeholder Feedback on Hypothetical First Spatial CDx Characteristics

Technology

- mIF or mIHC has the best chance of early success; spatial transcriptomics is regarded as too complex for clinical Dx

"…*mIF and mIHC are the future of CDx. With the help of DP and ML, there could be an assay on the market in the next 5 years*…"

-Executive Director of Biomarkers and CDx, Small Pharma, U.S.

Plex

- A panel of <5 plex, with well-validated analytes, the lower the plex, the higher the likelihood of adoption

"…*Anything looking at 8+ markers is discovery work. When it comes to the clinic, history shows that it should be 4-plex or less*…"

- Senior Director Clinical Biomarker Innovation & Development, Large Pharma, U.S.

Workflow

- A straightforward assay; likely and end-to-end solution that incorporates some level of automation in the workflow

"…*Clinicians need simplicity. Without it, I don't see spatial technology being used for clinical diagnostics*…"

- Computational Biologist, AMC, U.S.

Application

- The primary focus will be in immuno-oncology, most likely for use with a checkpoint inhibitor or combination therapy

"…*The immune response is inherently spatial, so it only makes sense to use diagnostics which indicatively utilize that information*…"

- Professor, AMC, U.K.

Indication

- Driven by the use-case, indications which are considered "hot" tumors from an immune infiltration perspective, such as lung, melanoma will likely see the first CDx

"…*The use of spatial will depend on the indication. Expect the usual suspects to see the initial spatial diagnostic activity*…"

- Executive Director, Large Pharma, U.S.

Reporting

- The data will need to be reported in a format that is easy to interpret, with clear and actionable results

"…*The results need to be actionable and easy to understand. The assay will need to have an AI backbone to tell clinicians yes or no*…"

- Professor, AMC, U.S.

The spatial biology market is expected to continue to maintain high growth beyond the forecast window of this report (e.g., 2027) as clinical applications come online

General Adoption of Spatial Biology*

Scope of Report ('22- '27)   Future Market Upside

| 2018 | 2022 | 2025 - 2026 | 2029+ |

A. Basic Discovery

- The integration of spatial biology into academic and biopharma discovery research has allowed for initial validation that the tech enables better understanding of the underlying biology and pathology; most large pharma and AMCs have leveraged spatial analysis for basic research in some capacity

B. Translational Research to Prospective Clinical Trials

- Today and in the near-mid term, most spatial biology activity will be in the translational and clinical research segments

- Discoveries / hypotheses from basic research will be validated in human clinical samples (and likely de-plexed) and associated with outcomes

  o This is done in the form of small, retrospective studies today, but will increasingly shift into larger, prospective studies as signals are further validated and technologies become more scalable (e.g., cost, automation) and validated

C. CDx Approval / Early Clinical Adoption

- With pharma now beginning to implement spatial in pivotal trials, the clinical data needed to support CDx approvals is likely ~4 years away, though some LDT offering may be used clinically before then

- Uptake in the clinic is likely to be limited to select applications / indications initially, however, the infrastructure and policies developed to accommodate these initial use-cases will "prime the channel," facilitating the adoption of subsequent tests

D. Routine Clinical Use

- The accumulation of CDx indications, especially any multi/pan-tumor indication, will make spatial analysis part of the standard-of-care for many patients (2029+)

  o Clinicians have shown willingness to rapidly adopt new Dx modalities / applications that have clinical value into routine practice (e.g., MRD)

- Adoption is expected to remain mostly centralized

Notes: * Timeline included for illustrative purposes – not to scale
Source: DeciBio Analysis

Agenda

- Introduction & Methodology
- Executive Summary
- Market Analysis
- Publication Analysis
- Primary Market Research
- **Competitive Analysis**

The following profiles contain secondary information as well as a DeciBio assessment of positioning; relative scoring is used such that leaders receive a 3

Spider Graph Key
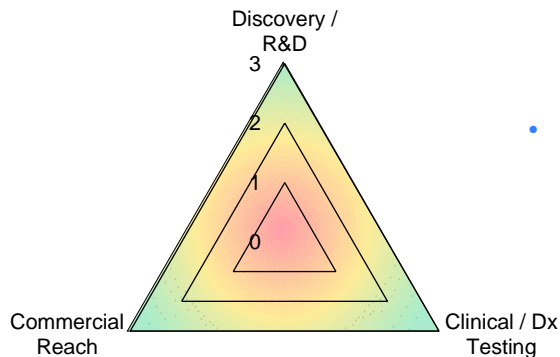
These are examples, and not all parameters apply to every company, scoring based on DeciBio's judgement and interviewee feedback

- 0 = N/A
- 1 = Trailing
- 2 = Competitive
- 3 = Leading

- **Discovery / R&D:**

    1. Low-plex, single-omics, seldom mentioned in discovery applications in primary research, low publication activity

    2. Mid-plex, mentioned in discovery applications in primary research, mid-level publication activity

    3. Highest plex / multi-omics capabilities, most often discussed in discovery applications in primary research, highest publication activity

- **Clinical / Dx Testing:**

    1. Low-level clinical-commercial activity, seldom mentioned in clinical / diagnostic applications in primary research, minimal clinical / Dx experience on team, high cost / low throughput solution

    2. Mid-level clinical-commercial activity (e.g., early (C)Dx partnerships, active communication of Dx aspirations), mentioned in clinical / diagnostic applications in primary research, some clinical / Dx team expertise, moderate cost / throughput

    3. High clinical-commercial activity, most often discussed in clinical / diagnostic applications in primary research, multiple and/or active / ongoing (C)Dx partnerships, some clinical / Dx certification or validation (e.g., CLIA lab status, analytical assay validation, strong clinical / Dx expertise on team, low cost / high throughput solution

- **Commercial Reach**:

    1. Low installed base or existing customers, limited international reach, small or non-existent commercial team, limited funding

    2. Moderate installed base / existing customers, moderate international reach, commercial team, and funding

    3. Significant install base / existing customers, high international reach, strong commercial team, significant funding / sales / resources

Akoya is a market-leading mIF provider with strong clinical focus, whose recent rebranding aims to streamline diagnostic development

DeciBio Analysis

Akoya offers comprehensive end-to-end spatial solutions across the R&D development timeline, and is currently focused on enhancing workflow speed, expanding its biomarker menu, and entering the clinical market; Akoya is a top mIF provider to date; Akoya continues tech evolution with the recently launched Fusion platform offering tunable plex, higher throughput, and multi-omic capabilities via a Bio-Techne collab; Akoya shows significant partnering activity to build a spatial biology ecosystem and drive platform adoption; their internal CLIA lab service offering supports the initial development phase of the first formal CDx partnership with Acrivon

Forward-Looking Positioning*
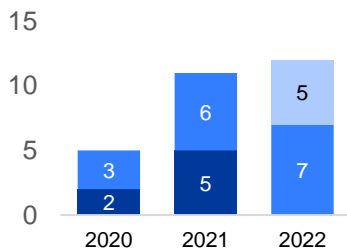
- 0 = N/A
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- 3 = Leading

Activity Snapshot**

■ Trials ■ Abstracts ■ Other

Key Activity Overview^

Click icon to follow link to activity

Icon	Company	Activity
Partnership	Acrivon	**Acrivon:** Jun 2022, CDx for ACR-368 via PhenoImager
Product Launch	PhenoCycler-Fusion	**PhenoCycler-Fusion:** April 2022, data showcase, re-brand, E2E workflow
Partnership	iCura	**iCura Dx:** Apr 2022, designation as qualified CRO
Partnership	bio-techne	**Bio-Techne:** Jan 2022, integration with RNAScope
Partnership	PathAI	**PathAI:** Dec 2021, AI biomarker discovery focus
Partnership	AstraZeneca	**AstraZeneca:** Jun 2021, translational I/O focus
Partnership	Oxford Instruments Andor, CrestOptics, Nikon	**Nikon**, **CrestOptics** and **Andor:** Jun 2021, CODEX integration with I² Network
Partnership	Johns Hopkins University	**Johns Hopkins:** Mar 2021, I/O biomarkers via AstroPath platform
Partnership	UCSF	**UCSF:** Jul 2020, I/O biomarker focus
M&A	PerkinElmer	**Phenoptics:** Oct 2018, acquired from PerkinElmer

Partnership   M&A   Product Launch

Akoya's offerings are competitively favorable, and the PhenoImager product is well-suited for clinical trial support

Products and Services Offered		
	Name / Description	**Competitive Analysis**
Instruments	• **PhenoCycler** (*prev. CODEX*): automated *in-situ* cycling platform (compatible with standard microscopes, incl. confocal), protein/RNA*, 100+ plex, 10-30 samples/week, FF/FFPE • **PhenoImager** (*prev. Phenoptics*): high-speed multispectral imaging platform, protein/RNA*, 6+ plex, single-cell/subcellular (down to 250 nm), 100 samples/week, FF/FFPE • **PhenoCycler-Fusion** combines PhenoCycler and PhenoImager into an E2E solution for spatial phenotyping; flexible tuning from high-plex to high-throughput**; single cell to subcellular resolution	+ Tunable plex-throughput configurations for discovery, translational and clinical applications + WSI imaging for unbiased tissue phenotyping down to sub-cellular resolution + Automated workflow-enabled; sample preserved + Moderate install base of PhenoImager systems (Vectra Polaris)
Reagents	• PhenoCycler (prev. CODEX)-conjugated Abs (mIF); Opal antibodies (PhenoImager, mIF); Universal Chemistry (*in dev.*); compatible with RNAScope HiPlex v2 for RNA detection	+ Off-the shelf & custom panels, validated antibodies available - Proprietary reagents, Ab conjugation required (PhenoCycler)
Bioinformatics	• Internal software for image management (Proxima), WSI (Phenochart), IA (inForm) and reporting (phenoptrReports); IA integration with Visiopharm and Indica Labs offerings	+ E2E solution with integrated bioinformatics + Open to 3rd party integration for downstream analysis
Services	• Internal CLIA-certified lab offers Advanced Biopharma Solutions (ABS) that include custom assay development, proprietary IA and CDx development	+ Enables initial phases of CDx co-development with pharma partners

Key Trials / Studies	Technology	Description
I-SPY 2 / NCT01042379: Recruiting | Comp: Dec 2031	mIF (PhenoImager)	Biomarkers of response to neoadj. I/O therapeutics in breast cancer | Ph 2 | 4,000 pts | Retrospective (UCSF collab.)
NCT02785250: Active | Comp: May 2025	mIF (PhenoImager)	Biomarkers of response to Maveropepimut-S (DPX-Survivac) in ovarian cancer | Ph 1|2 | 85 pts | Retrospective^
NCT04688658: Recruiting | Comp: Oct 2027	mIF (PhenoImager)	Biomarkers of response to Duvelisib / Nivolumab combination in Melanoma | Ph 1|2 | 42 pts | Prospective
NCT04963283: Recruiting | Comp: Feb 2025	mIF (PhenoImager)	Biomarkers of response to Cabozantinib / Nivolumab combination in colorectal cancer | Ph 2 | 46 pts | Prospective
Phase II Master Protocol: Planned | Comp: N/A	mIF (PhenoImager)	Patient stratification via OncoSignature ACR-368 CDx in ovarian, endometrial, urothelial | Ph 1|2 | N/A | Prospective
MITRE / Taube et al., 2021 (PMID: 34266881)	mIF (PhenoImager)	Multi-site mIF standardization study across 6 academic and pharma institutions

Notes: * PhenoCycler-Fusion workflow is compatible with the RNAScope HiPlex v2 assay; ** Fusion upgrade that doubles throughput expected by YE 2022; ^ CT.gov mentions TIL measurement, but does not specify method
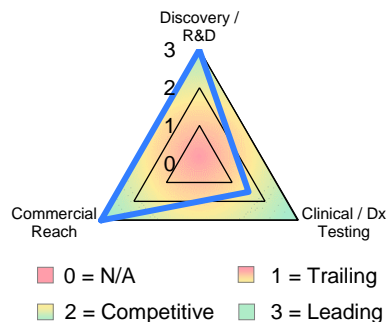Source: DeciBio Analysis

NanoString is a leader in spatial transcriptomic activity with strong presence in academia as a discovery tool
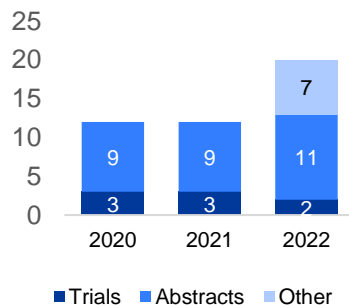
DeciBio Analysis

NanoString is a tools provider working to deliver a menu of end-to-end solutions for unbiased multi-omic spatial phenotyping at scale; considered the market leader in the academic spatial biology market; discovery-focused, but looking to expand further into the translational market segment; currently evolving the product portfolio and building an ecosystem of end-to-end solutions with workflow and bioinformatics automation through internal developments and diagnostics partnerships; strong R&D capabilities, but lack of clinical diagnostics testing capabilities to date; high publication and conference activity in both oncology and non-oncology applications

Forward-Looking Positioning*

Discovery / R&D, Clinical / Dx Testing, Commercial Reach

- 0 = N/A
- 1 = Trailing
- 2 = Competitive
- 3 = Leading

Activity Snapshot**

	2020	2021	2022
Other			7
Abstracts	9	9	11
Trials	3	3	2

■ Trials ■ Abstracts ■ Other

Click icon to follow link to activity

Key Activity Overview

CosMx SMI: Expected launch Fall 2022, high-plex *in situ* analysis platform providing spatial multi-omics

AtoMx SIP: Commercial unveiling June 2022, bioinformatics portal

BioChain: Apr 2022, qualified CRO

Leica: Feb 2022, workflow automation, Bond Rx autostainer

Illumina: Aug 2020, NGS readout for GeoMx; March 2022, cloud-based analytics, DRAGEN Bio-IT platform

Abcam: Apr 2019, Abs for GeoMx

GeoMx DSP: March 2019, flexible and robust spatial biology solution

Partnership   M&A   Product Launch

In a 2022 Q2 earnings call, NanoString CEO Brad Gray mentions that 2/3 GeoMx placements are with translational researchers, though the whole transcriptome assays that are often run on the GeoMx platforms are associated more closely with discovery work; additional comments at UBS mention ~75% academic GeoMx instrument placements

Notes: * Competitive positioning indicates readiness for future developments in a particular area, see structure on slide 46; ** Company activity counts include only activity explicitly related to spatial biology; ^ Top activity prioritized via presence of biomarker-matched clinical outcomes data, journal impact factor, and are ultimately subject to DeciBio writer discretion

Source: DeciBio Analysis

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49

NanoString's GeoMx platform pushes toward clinical research, but proprietary technology and workflow complexity reinforce its translational positioning

Products and Services Offered

	Name / Description	Competitive Analysis
Instruments	• **GeoMx DSP**: imager and molecular profiler (compatible with nCounter and NGS readouts), RNA/protein, ~18,000-plex (RNA) / 140+ plex (protein), multi-cell/single-cell (ROI, 1 μm), 10 slides per day*, FF/FFPE • **CosMx SMI****: automated cyclic *in-situ* imager (smFISH), RNA/protein, up to 1000-plex (RNA) / 100-plex (protein), single-cell/subcellular, tunable from high-plex to high-throughput, FF/FFPE	+ Ultra-high plex available for discovery applications + Tunable plex-throughput configurations (CosMx) + Sample preserved - Workflow complexity; high CapEx - GeoMx not considered true single-cell
Reagents	• Off-the-shelf and custom RNA and protein panels, incl. Cancer Transcriptome Atlas (CTA, ~1,800 RNA), Whole Transcriptome Atlas (WTA, ~18,000 RNA), IO and Neurobiology protein panels	+ Large off-the-shelf menu, customization available + Proven multi-omic detection capability - Proprietary reagents
Bioinformatics	• Internal: AtoMx Spatial Informatics Portal (SIP) expected to launch Fall 2022, cloud-based solution for IA, DA, visualization, global collaboration, storage • 3rd party: GeoMx workflows available on Illumina's DRAGEN Bio-IT platform for secondary DA	+ E2E solution with integrated bioinformatics + Open to 3rd party integration for downstream analysis
Services	• Technology Access (TAP) and Data Analysis (DAS) for pilot studies / technology evaluation	- No internal CLIA-certified laboratory for clinical applications

Key Trials / Studies^	Technology	Description
FinXX / NCT00114816: Completed | Comp: 4/07	GeoMx	Prognostic biomarker discovery in breast cancer patients treated w/ 2 chemo regimens | Ph 3 | 1,500 pts | Retrospective
NCT02731729: Completed | Comp: 2/19	GeoMx	Exploratory biomarker profiling of immune checkpoint inhibitor-treated melanoma | Ph 2 | 20 pts | Retrospective
NCT02923180^^: Active | Comp: 9/22	GeoMx	Longitudinal biomarker analysis of response to enoblituzumab in prostate cancer | Ph 2 | 33 pts | Retrospective
NCT04895761: Recruiting | Comp: 6/26	GeoMx	Safety (immunogenicity) neoadjuvant aromatase inhibitor in breast cancer | Ph 1b | 18 pts | Prospective
Moutafi et al., 2022 (PMID: 35490853)	GeoMx	Biomarker discovery using the protein-based molecular compartmentalization in NSCLC patients treated w/ ICI | Retrospective

Notes: * Throughput from 2021 NanoString 10-K filing; ** Currently available through TAP, full commercial launch in Q4 2022; ^ 223 GeoMx/CosMx publications listed on the company website; ^^ Additional biomarker information for this trial here
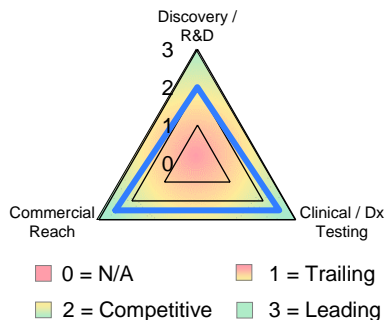
Source: DeciBio Analysis

With a reagent-only offering, Ultivue may see gated adoption in later translational work where the customizability of the workflow presents standardization issues

DeciBio Analysis

Ultivue is a spatial biology reagents provider that offers platform-agnostic low-to-mid plex mIF kits; Ultivue is expanding their offering through image analysis services and AI partnering; activity is centered around building ecosystem partnerships for a modular end-to-end offering for spatial phenomics; Ultivue is currently R&D focused, but reagents are well suited for translational research and, ultimately, diagnostics; internal CLIA-lab and qualified specialty CRO partnerships support expansion of InSituPlex reagent utilization for MTA biomarker development and clinical applications; decentralizability, customizability, and openness are key differentiators

Forward-Looking Positioning*

- 🔴 0 = N/A
- 🟠 1 = Trailing
- 🟡 2 = Competitive
- 🟢 3 = Leading

Activity Snapshot**

- ■ Trials
- ■ Abstracts
- ■ Other
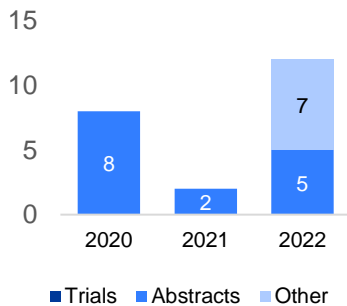
Key Activity Overview

Click icon to follow link to activity

🤝	nucleai	**Nucleai:** Jun 2022, AT platform provider
🤝	zegami	**Zegami:** May 2022, AI platform provider
🤝	Paige	**Paige:** Apr 2022, AI platform provider
🚀		**FlexVUE panels:** Apr 2022, 4- or 8-plex mIF
🤝	KeenEye	**KeenEye:** Mar 2022, AI platform provider
🤝	AIGNOSTICS	**Aignostics:** Mar 2022, AI platform provider
🤝	Sirona Dx	**Sirona Dx:** Mar 2022, qualified CRO
🤝	FLUIDIGM	**Fluidigm:** Aug 2021, co-marketing with IMC products
🤝	VISIOPHARM	**Visiopharm:** Mar 2021, IA for I/O panels
🤝	OracleBio	**OracleBio:** Jul 2020, qualified CRO
🤝	Leica BIOSYSTEMS	**Leica:** Oct 2018, co-marketing with BOND RX
🤝	indica labs	**Indica Labs:** Sep 2018, IA, initially through IDS

🤝 Partnership 🔲 M&A 🚀 Product Launch

Notes: * Competitive positioning indicates readiness for future developments in a particular area, see structure on slide 46; ** Company activity counts include only activity explicitly related to spatial biology; ^ Top activity prioritized via presence of biomarker-matched clinical outcomes data, journal impact factor, and are ultimately subject to DeciBio writer discretion

Source: DeciBio Analysis

Ultivue's InSituPlex offerings are well-suited for diagnostics, though the relative limitation in plex may moderate adoption during the discovery phase

Products and Services Offered		
	Name / Description	Competitive Analysis
Instruments	• No internal instrument offering	+ Compatible with standard microscope detection - Demonstration of compatibility with workflow components required
Reagents	• Ready-to-use (FixVUE, 4- and 8-plex) and customizable (FlexVUE and U-VUE) mIF panels utilizing **InSituPlex** technology (up to 12-plex*, same slide-H&E), optimized for the BOND RX autostainer • Working on multi-omic detection capabilities (initially available as a service offering)	+ Off-the-shelf menu and various levels of customization available + Platform agnostic, able to plug into standard laboratory workflows + Sample preserved - Currently protein detection only - Lower plex compared to research-oriented proteomics tools
Bioinformatics	• Internal: UltiStacker software (image alignment/initial processing) • Partner offerings for downstream IA/DA	+ Open to 3rd party integration for downstream analysis, various image analysis partnerships in place - Limited internal bioinformatics
Services	• Internal CLIA-certified lab offers custom assay development, staining, imaging (IDS) and clinical trail services	+ Enables initial phases of CDx co-development with pharma partners

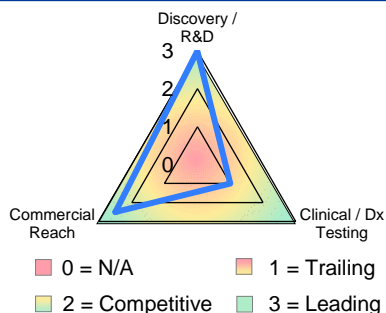| Key Trials / Studies	Technology	Description
AACR 2022 – 3868 / 13	mIF (FlexVUE)	Introduction to novel 8-plex FlexVUE mIF panels coupled to UltiStacker software for TIME analysis
AACR 2022 – 3866 / 11	mIF (InSituPlex)	Demonstration of Ultivue InSituPlex integrated workflow for co-detection of protein and RNA; workflow automation with Leica Biosystems BOND RX autostainer and Indica Labs HALO analyitics
AACR 2022 – 1709 / 6	mIF (InSituPlex)	Exploratory tissue phenotyping workflow combining 4-plex InSituPlex PD-L1 mIF panel, 40-plex IMC panel (Standard Biotools) and Visiopharm IA to study the TME in PDAC
Montanari et al. 2022 (PMID: 35218813)	mIF (InSituPlex)	Exploratory analysis of human liver correlates leukocyte infiltration with chronic HBV

Notes: * InSituPlex technology is available in 4, 8, 12-plex panel options; ^ Internal service lab utilizes Zeiss Axioscan for whole slide scanning and imaging;
Source: DeciBio Analysis

52

10X Genomics is quickly growing its presence in spatial transcriptomics, particularly in academic labs and earlier stage translational work; it has a large research footprint

DeciBio Analysis

10X Genomics is a tools provider leveraging market leadership and sales channels in single-cell genomics to expand into spatial biology; currently focused on growing its product portfolio of integrated solutions for unbiased discovery applications; 10x spatial capabilities were developed though in-licensing / M&A; key spatial activity includes evolving the flagship Visium spatial product line with FFPE compatibility, automated sample prep, improved resolution, integrated bioinformatics and multi-omic detection; next steps are developing a turnkey spatial phenotyping solution to address emerging translational / clinical market needs w/ Xenium *in situ* E2E platform

Forward-Looking Positioning*

- ■ 0 = N/A
- ■ 1 = Trailing
- ■ 2 = Competitive
- ■ 3 = Leading

Activity Snapshot**

■ Trials ■ Abstracts ■ Other
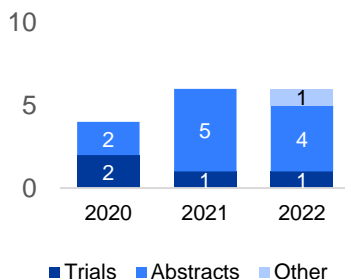
Key Activity Overview

Click icon to follow link to activity

Visium HD, Xenium *in situ* **platform**: YE'22		
Visium CytAssist: mid-2022, automated sample processing		
Expanded CSP network of CROs: Jan 2022		
Visium FFPE: June 2021, whole transcriptome analysis		
Tetramer Shop: Feb 2021, T-cell detection		
PICI: Jan 2021, IO research		
ReadCoor: Oct 2020, *in situ* FISSEQ		
Cartana: Sep 2020, *in situ* sequencing		
Visium: Nov 2019, spatial gene expression data analysis / visualization tools		
Spatial Transcriptomics: Dec 2018, Visium tech		
Epinomics: Aug 2018, ATAC-seq tech		
Illumina: Feb 2016, Long read application		

🤝 Partnership   🧩 M&A   🚀 Product Launch

Notes: * Competitive positioning indicates readiness for future developments in a particular area, see structure on slide 46; ** Company activity counts include only activity explicitly related to spatial biology;
         ^ Top activity prioritized via presence of biomarker-matched clinical outcomes data, journal impact factor, and are ultimately subject to DeciBio writer discretion
Source: DeciBio Analysis

10x's Visium platform has helped its push toward clinical research, though high price and immense data creation maintains its discovery positioning

Products and Services Offered		
	Name / Description	**Competitive Analysis**
Instruments	• No instrument required: Visium reagents compatible with 3rd party NGS instrument readout • **Visium CytAssist** for automated sample processing • **Xenium** (technology access in 2022, commercial launch in 2023): *in situ* imaging platform, RNA/protein, subcellular, high-throughput, FF/FFPE	+ Limited amount of CapEx required for the Visium product line - Workflow complexity (CytAssist to drive simplification) - Destructive technology (sample not preserved)
Reagents	• **Visium** (4x*, multi-cell ROI, 50 μm), Visium FFPE, Visium HD (improved resolution, 1,500x) for whole transcript. analysis, low throughput (spatial gene expression reagents & slide kits) • High parameter multi-omic offering (incl. protein co-detection) in development	+ Ultra-high plex for unbiased spatial profiling + Fresh-frozen and FFPE compatible + Supports RNA + protein analysis**
Bioinformatics	• Visium Spatial Gene Expression Software Suite, incl. Space Ranger (initial analysis) and Loupe Browser (visualization and downstream analysis); 10x Genomics Cloud platform for data management, analysis, and collaboration (*currently supports single-cell data only*)	+ Integrated bioinformatics offering - Visium not considered true single-cell
Services	• No internal service offering • Certified Service Provider (CSP) Network (incl. Q² Solutions, Azenta Life Sciences, CellCarta)	+ Large qualified CRO network available to support large-scale clinical trails for pharma partners - No internal service lab for pilot projects

Key Trials / Studies^	Technology	Description
LiMeT / NCT04622423: Recruiting | Comp: 06/26	Spatial Transcript.	Evaluation of molecular and cellular composition of CRC and PDAC liver MTS by spatial transcriptomics technologies (NICHE-seq and Visium)^^ | Observational | 475 pts | Prospective
TIOB / NCT05371756: Recruiting | Comp: 09/52	Spatial Transcript.	Collection of patients' biospecimens for Texas Immuno-Oncology Biorepository (TIOB) | Observational | 100,000 pts | Prospective
SITC 2021 – 83	Spatial Transcript.	Multi-omic tumor analyses of breast cancer samples with Visium FFPE with multiplex protein enablement (IO antibody panel developed with Abcam conjugated antibodies)
AACR 2022 – 2130	Spatial Transcript.	Novel bioinformatics pipeline to infer molecular changes from tumor & immune cell interactions in the TME from Visium ST data

Notes: * Resolution defined as number of spots per unit area; ** Compatible with immunofluorescence staining / imaging upfront of Visium spatial gene expression workflow; ^ 104 spatial gene expression publications listed on the company website; ^^ Study also lists spatial proteomics technologies, such as GeoMx DSP (NanoString), for sample characterization

Source: DeciBio Analysis

Standard Biotools supports discovery and early-stage clinical research via their high-plex, high-cost imaging mass cytometry platform

DeciBio Analysis

Standard Biotools is a life science research tools provider (formerly known as Fluidigm) with a low-moderate throughput, high-plex spatial proteomics solution sees lower activity versus other spatial biology providers; imaging mass cytometry (IMC) technology is used largely for exploratory applications, but has been deployed prospectively in early-stage trials; Standard Biotools is building an integrated tissue phenotyping workflow with IMC profiling and 3rd party analytics; commercial reveal of the next generation IMC instrument with higher throughput and sensitivity at AACR 2022; looking to re-invigorate and expand the product portfolio by acquiring de-risked complementary assets
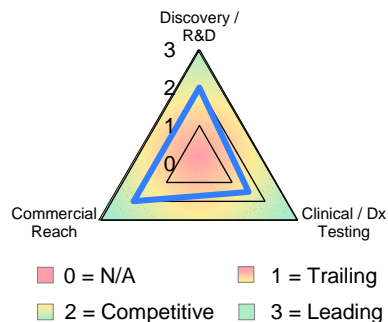
Key Activity Overview

Click icon to follow link to activity

🚀	＋	**Hyperion+:** April 2022 commercial reveal, next-gen IMC instrument
🤝	VISIO PHARM	**Visiopharm:** Oct 2021, IA
🤝	ImaBiotech — Revealing Biological Secrets	**ImaBiotech:** Aug 2021, qualified CRO
🤝	U Ultivue	**Ultivue:** Aug 2021, co-marketing for InSituPlex products
🤝	indica labs	**Indica Labs:** Feb 2019, IA
🚀		**Hyperion Imaging System:** Oct 2017, IMC platform

🤝 Partnership   M&A   🚀 Product Launch
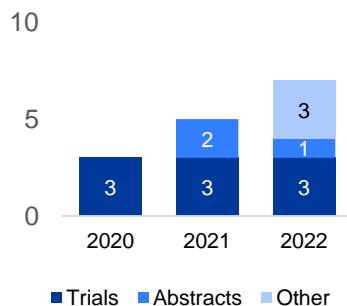
Forward-Looking Positioning*

Discovery / R&D

Commercial Reach — Clinical / Dx Testing

- 0 = N/A
- 1 = Trailing
- 2 = Competitive
- 3 = Leading

Activity Snapshot**

Year	Trials	Abstracts	Other
2020	3		
2021	3	2	
2022	3	1	3

■ Trials ■ Abstracts ■ Other

New instruments offered by Standard Biotools address throughput issues, increasing the potential for clinical research use

Products and Services Offered		
	Name / Description	**Competitive Analysis**
Instruments	• **Hyperion Imaging System**: imaging mass cytometry (IMC) platform*, up to 40-plex, single-cell (1 µm), low-to-medium throughput (ROI-based, 1 mm^2 / ~2 hours)**, FF/FFPE • **Hyperion+**: next-gen IMC instrument, protein, 40+ plex, subcellular, 2x higher throughput (100 samples/week)^, improved sensitivity (up to 1.6x LOD improvement), FF/FFPE	+ Higher throughput relative to other high-plex methods - Large CapEx required - Destructive technology (sample not preserved)
Reagents	• **Maxpar** metal-conjugated antibodies^^ and kits • Custom antibody labeling service	+ Capable of ~40-plex proteomic analysis + Custom and off-the-shelf options - Proprietary reagents, Ab conjugation required - Protein-only detection
Bioinformatics	• Internal: CyTOF Software 7.0 (initial analysis), MCD Viewer, histoCAT (downstream analysis) • 3rd party secondary analysis (Visiopharm and Indica Labs)	+ Open to 3rd party integration for downstream IA/DA - Internal bioinformatics perceived as insufficient
Services	• PRO Services (incl. custom conjugation and assay design, scientific consultation, laboratory optimization)	- No internal CLIA-certified laboratory for clinical applications

Key Trials / Studies†	Technology	Description
NCT03299946: Completed | Comp: 10/21	IMC	Biomarkers of response to neoadj. Cabozantinib / Nivolumab combination in HCC | Ph 1b | 15 pts | Retrospective
ATRiUM / NCT03669601: Recruiting | Comp: 9/24	IMC	Biomarkers of response to Ceralasertib / Gemcitabine combination in AST | Ph 1 | 55 pts | Retrospective
PICT-01 / NCT04009967: Recruiting | Comp: 5/23	IMC	Biomarkers of response to neoadjuvant Pembrolizumab in prostate cancer | Ph 2 | 30 pts | Prospective
NCT04393285: Active | Comp: 9/24	IMC	Biomarkers of response to Abemaciclib / Letrozole combo in endometrial cancer | Ph 2 | 50 pts | Prospective
NCT04951154: Recruiting | Comp: 6/25	IMC	Expl. biomarker analysis in untreated NSCLC bronchoscopic biopsies | Observational | 50 pts | Prospective

Notes: * Imaging module connected to the Helios mass cytometer system; ** ROI-based throughput figure via *Baharlou 2019* ^ 100 samples per week via company website; ^^ Off-the-shelf catalog of > 800 metal-conjugated antibodies (no autofluorescence); † >130 publications utilizing IMC technology referenced on the company website
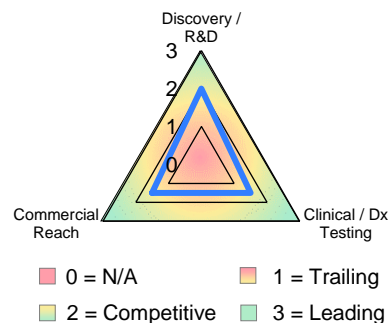
Source: DeciBio Analysis

IONpath offers the discovery-enabling high-plex IMC platform MIBIscope, which shows lower activity than other IMC platforms
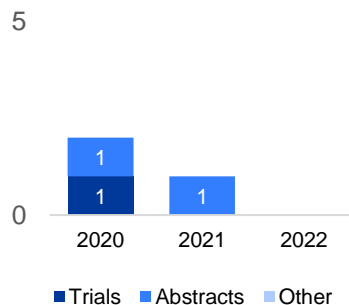
DeciBio Analysis

Early-stage spatial proteomics platform and service provider commercializing Multiplexed Ion Beam Imaging (MIBI) technology for high-definition spatial analysis of the tissue microenvironment; Offers MIBIscope instruments and reagents, as well as an internal end-to-end spatial proteomics service for biopharma immuno-oncology applications; Low level of conference and publication activity; Recent strategic investment by Thermo to continue to scale the organization; Focused on the near-term potential of spatial proteomics in oncology biomarker development and diagnostics

Forward-Looking Positioning*

Discovery / R&D

Commercial Reach — Clinical / Dx Testing

- 0 = N/A
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- 3 = Leading

Activity Snapshot**

5

0

| | 2020 | 2021 | 2022 |

- Trials
- Abstracts
- Other

Key Activity Overview

Click icon to follow link to activity

🤝	**Thermo Fisher SCIENTIFIC**	**Thermo Fisher Scientific:** May 2022, Strategic Investment
🚀		**MIBIscope:** Nov 2019, multiplexed ion beam imaging system
🤝	**indica labs**	**Indica Labs:** Apr 2019, IA

🤝 Partnership   🧩 M&A   🚀 Product Launch

Notes: * Competitive positioning indicates readiness for future developments in a particular area, see structure on slide 46; ** Company activity counts include only activity explicitly related to spatial biology; ^ Top activity prioritized via presence of biomarker-matched clinical outcomes data, journal impact factor, and are ultimately subject to DeciBio writer discretion

Source: DeciBio Analysis

MIBIscope sees prospective use in NCI-led trials and has proven concordance to single-plex IHC up to 16-plex

Products and Services Offered		
	Name / Description	Competitive Analysis
Instruments	• **MIBIscope**: mass cytometry imaging platform (MIBI-TOF), protein, 40+ plex, subcellular (down to 350 nm)*, high-throughput (up to 90 800×800 µm^2 ROIs per day, 100s of samples/week), FF/FFPE	+ Single step high-resolution imaging for quantitative single-cell phenotype mapping + Reliability to run 24/7 enables studies on large clinical cohorts + Sample preserved
Reagents	• Pre-conjugated Abs (metal-tags, single-step standard IHC protocol) and Conjugation kits (MIBItag Conjugation Kits) • IO biomarker panels (30-marker Checkpoint Panel, validated add-on markers)	+ Off-the shelf validated reagents, customization available + Capable of ~40-plex proteomic analysis - Proprietary reagents, Ab conjugation required
Bioinformatics	• MIBItracker cloud-based data management and visualization platform • 3rd party downstream IA/DA (e.g., Fiji, HALO (Indica Labs), VisioPharm, QuPath)	+ Open to 3rd party integration for downstream IA/DA - Limited internal bioinformatics
Services	• In-house E2E service offering: Spatial Proteomic Services (Feb 2020, IO focus), Spatial Proteomics Pilot Program for biopharma R&D (Aug 2021, IO focus)	- No internal CLIA-certified laboratory for clinical applications

Key Trials / Studies	Technology	Description
NCT04053673**: Recruiting | Comp: Jan 2023	MIBI	Expl. analysis of the TME in ASTs treated with a PARP7 inhibitor RBN-2397 | Ph 1 | 130 pts | Retrospective
NCT04068194: Recruiting | Comp: Dec 2022	MIBI	Exploratory TIL biomarkers in Peposertib + Avelumab-treated patients with AST and Hepatobiliary Malignancies | Ph 1|2 | 39 pts | Prospective
Liu et al., 2022 (PMID: 35351966)	MIBI	NCI concordance study of MIBI-TOF and digitized, single-plex IHC for 16 targets
Risom et al., 2022 (PMID: 35063072)	MIBI	Application of 37-plex MIBI profiling of the TME in Ductal carcinoma in situ (DCIS)
Ptacek et al., 2020 (PMID: 32203152)	MIBI	Application of 15-plex MIBI profiling of the TME in FFPE samples (BMS collaboration, co-authored)

Notes: * Ability to scan the whole tissue section faster at low resolution, then re-scan ROIs at higher resolution; ** additional biomarker information here
Source: DeciBio Analysis

Vizgen recent commercial launch of MERSCOPE has moderated research and commercial activity to-date; multi-omic platform has generated significant hype

DeciBio Analysis

Spatial transcriptomics startup commercializing the recently-launched MERSCOPE platform based on Multiplexed Error-Robust Fluorescence In Situ Hybridization (MERFISH); represents the next generation of genomics tools, and expands on the capabilities of spatially-resolved transcriptomics with an automated high-resolution *in situ* platform; platform fit for discovery research applications, and suitable for large-scale transcriptomic projects (e.g. cell atlas generation); broad research applications beyond oncology with neurology case studies presented at recent conferences. Workflow automation and on-board analysis address key spatial biology needs / pain points raised by stakeholders
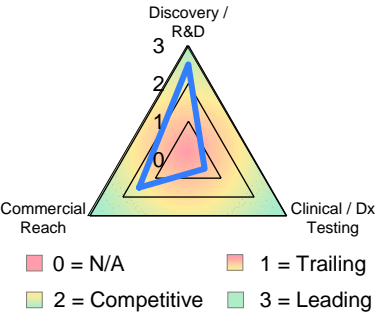
Click icon to follow link to activity
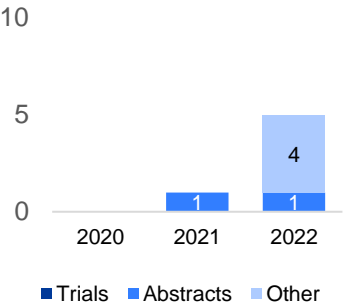
Key Activity Overview

MERSCOPE: Aug 2021 limited release, Jan 2022 broad US availability; high multiplexing, high resolution *in situ* platform combining single-cell and spatial genomics analysis

Partnership   M&A   Product Launch

Forward-Looking Positioning*

Discovery / R&D

Commercial Reach

Clinical / Dx Testing

- 0 = N/A
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- 2 = Competitive
- 3 = Leading

Activity Snapshot**

2020   2021   2022

■ Trials ■ Abstracts ■ Other

Notes: * Competitive positioning indicates readiness for future developments in a particular area, see structure on slide 46; ** Company activity counts include only activity explicitly related to spatial biology;
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Source: DeciBio Analysis

Presence at AACR and AGBT 2022 for MERFISH serves as proof of concept for high resolution spatial transcriptomics

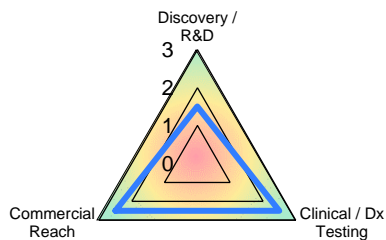| Products and Services Offered		
	Name / Description	Competitive Analysis
Instruments	• MERSCOPE: automated fluidics and imaging smFISH platform (MERFISH method exclusively licensed from Harvard University), RNA, up to 500-plex, subcellular (≤100 nm), high-throughput, FF currently, FFPE planned for H2 2022	+ High spatial resolution of 100s of RNA transcripts - Recent commercial availability, small installed base
Reagents	• MERSCOPE reagents: custom MERFISH gene panels in 3 sizes (up 140, 300 or 500 genes), 1000-gene panels planned for H2 2022 • Protein co-detection on roadmap (H2 2022)	+ Custom validated reagents - Proprietary reagents - Currently lacks multi-omic capabilities
Bioinformatics	• MERSCOPE Vizualizer software (and a free web-based version - MERSCOPE Web Vizualizer) for data visualization	- Limited internal bioinformatics
Services	• Lab services (in-house sample processing and data analysis)	- No internal CLIA-certified laboratory for clinical applications

Key Trials / Studies	Technology	Description
AACR 2022 – 2030 / 8	Spatial Transcriptomics (MERFISH)	Exploratory single-cell spatially-resolved 450+ plex MERFISH gene expression analysis in the TME of CRC samples (commercial or obtained through Massachusetts General Hospital (MGH)
AGBT 2022 – 593	Spatial Transcriptomics (MERFISH)	Demonstration of in situ single-cell transcriptomic Imaging in FFPE tissues with MERSCOPE (FFPE sample compatibility)

Leica Cell DIVE mIF offers flexibility via compatibility with third-party reagents and utilizes existing BOND RX equipment
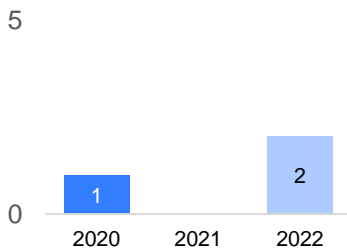
DeciBio Analysis

Microscope manufacturing company with a broad portfolio of microscopes and imaging systems; Cell DIVE cyclic multiplexed imaging platform is an open E2E system compatible with 3rd party reagents; Targeting the clinical market with spatial phenotyping and digital pathology solutions; Cell DIVE utilizes an established scalable mIF technology well suited for translational and clinical applications, but clinical adoption of the platform is lagging despite significant commercial reach via existing install base of scanners. Leica also has select multiplex IHC kit / reagent offerings. Leica can leverage its existing clinical Dx and DP presence to being spatial into the clinic.

Forward-Looking Positioning*

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- 1 = Trailing
- 2 = Competitive
- 3 = Leading

Activity Snapshot**

2020 | 2021 | 2022

- Trials
- Abstracts
- Other

Key Activity Overview

Click icon to follow link to activity

Icon	Company	Activity
M&A	Cell IDx	**Cell IDx, Inc.:** Nov 2022, UltraPlex mIF / mIHC kits to run on BOND RX platform
Partnership	indica labs	**Indica Labs**: Sep 2022, digital pathology workflow solutions
Partnership	nanoString	**NanoString:** Feb 2022, workflow automation, Bond RX autostainer
M&A	cytiva / DANAHER	**Cytiva:** Mar 2020, biopharma business of the GE Life Sciences division, acquired by Danaher*
Product Launch	Cell DIVE	**Cell DIVE:** Sep 2019, via acquisition of Cytiva
Partnership	Ultivue	**Ultivue:** Oct 2018, co-marketing with BOND RX
Partnership	ACD a biotechne brand	**ACD:** Jan 2016, automation partner (BOND III & RX)

- Partnership
- M&A
- Product Launch

Note: activity focuses on Leica Microsystems Cell DIVE offering, but includes some high-impact activity regarding Leica Biosystems' BOND RX platform

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Source: DeciBio Analysis

Research and clinical activity lack for Cell DIVE, which has likely fallen behind due to lack of extreme marketing efforts seen by other mIF players

Products and Services Offered		
	Name / Description	Competitive Analysis (Cell Dive)
Instruments	• Broad portfolio of microscopes • Digital pathology solutions (e.g., Aperio GT 450 digital pathology slide scanner) • **Cell DIVE**: automated multiplex imaging platform (cyclic imaging*, 4 Abs per cycle), protein, 60+ plex, single-cell (ROI-based, down to ~400 nm), high-throughput (whole slide in 2.25 hours, 45x20 mm area, 20x, 4-channels); FF/FFPE	+ Automated E2E platform for whole tissue imaging + Sample preserved + Scalability and flexibility of iterative staining/imaging approach - Throughput decreases with increased panel size
Reagents	• Compatible with 3rd party reagents (open platform) • Validated antibodies (350+) available for custom biomarker panel design • mIHC (3-4 plex) and mIF (4-plex) kits leveraging a novel chemistry for 1° antibody independent multiplexing; acquired from CellIDx; off-the-shelf kits and custom reagents	+ Open-source reagents + Proprietary multiplexing chemistry for both mIHC and mIF that is optimized for Leica's instruments - Protein-only detection
Bioinformatics	• Internal analysis software (primary analysis) • Downstream 3rd party analytics: HALO (Indica Labs)	+ Open to 3rd party integration for downstream IA/DA - Limited internal bioinformatics
Services	• No service offering	

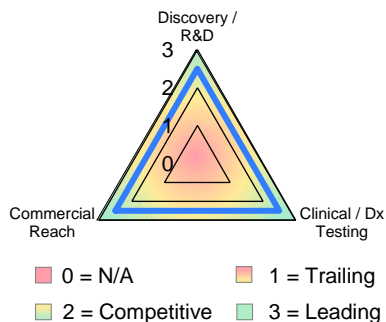| Key Trials / Studies	Technology	Description
Pachynski et al., 2021 (PMID: 33771855)	mIF (Cell DIVE)	Exploratory TME profiling in prostate cancer to determine spatial underpinnings of radiographic heterogeneity
Kanwar et al., 2021 (PMID: 34711609)	mIF (Cell DIVE)	Determination of intra-tumoral spatial heterogeneity and host immune response in the TME of breast cancer
Stachtea et al., 2021 (PMID: 34732839)	mIF (Cell DIVE)	Evaluation of immune signatures in the tumor / TME and their correlations with patient outcomes in CRC
Pourmaleki et al., 2022 (PMID: 35013003)	mIF (Cell DIVE)	Novel IO biomarker development via multi-omic evaluation of intralesional IL2 response in melanoma

Notes: * ClickWell slide carrier allows staining and dye inactivation solutions to be applied without placing or removing coverslips, ensuring minimal tissue damage over many rounds of imaging
Source: DeciBio Analysis

NeoGenomics is a leading spatial biology service provider which offers access to many platforms across the research continuum
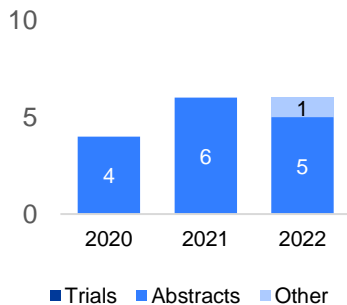
DeciBio Analysis

Largest oncology-focused U.S. CRO offering comprehensive biomarker testing services, including mIF profiling; global CAP-accredited / CLIA-certified lab network supporting oncology clinical trials; pharma services business offers 2 mIF platforms: internal MultiOmyx for high-order (≥ 7-plex) protein measurements and PhenoImager HT (Akoya) for low-order (2-6 plex) measurements; established partnership w/ NanoString offers use of DSP & additional platforms; Leader in mid-plex MTA service with advanced internal bioinformatics, including deep learning-based cell classification; partnership with Biognosys to expand multi-omic solutions for biopharma customers

Forward-Looking Positioning*

Discovery / R&D

Commercial Reach — Clinical / Dx Testing

- 0 = N/A
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Activity Snapshot**

2020	2021	2022
4	6	5 (+1)

■ Trials ■ Abstracts ■ Other

Key Activity Overview

Click icon to follow link to activity

Akoya: Current, end-to-end PhenoImager™ service solution using optimized / high-throughput workflow

Biognosys: Apr 2022, joint scientific / technical initiatives

Nanostring: Jul 2020, deliver analysis system and pharma services to oncologists

Clarient, Inc.: Dec 2015, acquisition, GE Healthcare

MultiOmyx: Feb 2013, protein characterization / visualization in FFPE tissue section

🤝 Partnership   🧩 M&A   🚀 Product Launch

Notes: * Competitive positioning indicates readiness for future developments in a particular area, see structure on slide 46; ** Company activity counts include only activity explicitly related to spatial biology;
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Source: DeciBio Analysis

MultiOmyx, a proprietary NeoGenomics platform, sees significant clinical use, while other platforms serve the discovery space

Products and Services Offered		
	Name / Description	Competitive Analysis
Instruments	• No instrument offering	
Reagents	• **MultiOmyx**: proprietary mIF staining protocol (cyclic imaging, 2 Abs per cycle), protein, up to 60-plex, single-cell, FFPE • Broad array of verified MultiOmyx panels (IO focused) • Custom assay design / verification • Integrated with FISH, RNAScope, and NGS	+ Comprehensive test menu, customization available + Standardized workflow + Sample preserved (non-destructive) + Multi-omic capabilities through platform integration - Only available as a service offering
Bioinformatics	• Internal IA / visualization tools • NeoVUE image and data visualization software for end-users • NeoLYTX internal DL-based cell classification platform (optimized for MultiOmyx, RUO)	+ Advanced internal bioinformatics, including AI
Services	• Pharma services* offered through an internal network** of CAP-accredited, CLIA-certified labs; wide array of instruments / methods (e.g., NanoString DSP, Akoya PhenoImager, RNAscope) • Include CDx services (from assay development through commercialization)	+ Clinical CRO capabilities available for biopharma partners + CDx development and commercialization expertise

Key Trials / Studies	Technology	Description
NCT02528357: Completed | Comp: May 2021	mIF (MultiOmyx)	Biomarkers of response to GSK3174998 ± pembrolizumab in ASTs | Ph 1 | 141 pts | Retrospective
NCT03291002: Active | Comp: Feb 2023	mIF (MultiOmyx)	Exploratory TME characterization following intra-tumoral CV8102 in solid tumors | Ph 1 | 98 pts | Retrospective
NCT03506373: Active | Comp: May 2025	mIF (MultiOmyx)	Exploratory TIL immunophenotyping of effects of ibrutinib + ixazomib on the TME in WM patients | Ph 2 | 23 pts | Prospective
NCT05163041: Recruiting | Comp: May 2025	mIF (MultiOmyx)	Monitoring of Nectin-4 and CD137 expression in BT7480-treated ASTs | Ph 1|2 | 200 pts | Prospective^
AACR 2021 – 2681	mIF (MultiOmyx)	Integration with RNAscope (ACD) RNA profiling for multi-omic analysis of the TME in NSCLC
AACR 2022 – 33801 / 1	mIF (MultiOmyx)	Integration with GeoMx spatial transcriptomics (NanoString) for multi-omic analysis of CRC-associated IBD

Notes: * Pharma Services offer two mIF platforms: MultiOmyx (internal, ≥ 7plex) and PhenoImager HT (Akoya, 2-6plex); ** internal network of 14 global locations; ^ Likely prospective, as MultiOmyx deployment in BT7480 FIH clinical trial mentioned in *SITC 2021 – 2*
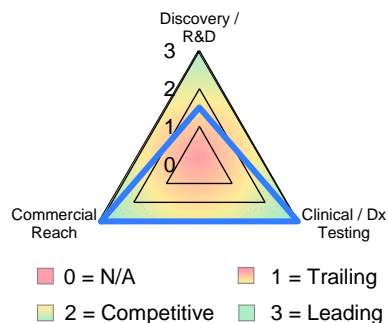
Source: DeciBio Analysis

As a legacy player in spatial transcriptomics, Bio-Techne / ACD sees large market share and high utilization with low per-sample costs for low-plex (duplex) assays
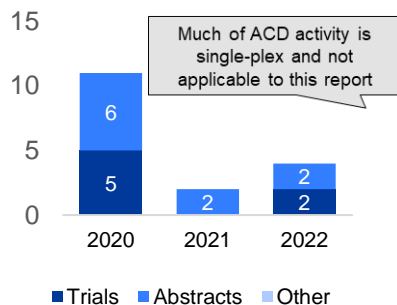
DeciBio Analysis

Reagents and services provider for *in situ* genomic analysis commercializing RNA-ISH technology for biomarker applications in both the research and the diagnostic markets; established solutions for tissue-based gene expression analysis supporting a broad range of pre-clinical and clinical applications in every therapeutic area; Technology is CE-IVD marked for clinical diagnostic use in Europe; building E2E multi-omic solutions through workflow automation and downstream analytics partnerships; biopharma-focused internal service offering provides E2E biomarker assay development / validation and CDx development

Forward-Looking Positioning*

Legend:
- 0 = N/A
- 1 = Trailing
- 2 = Competitive
- 3 = Leading

Activity Snapshot**

Callout: Much of ACD activity is single-plex and not applicable to this report

Legend: ■ Trials ■ Abstracts ■ Other

Key Activity Overview

Click icon to follow link to activity

🤝	NEO GENOMICS / Flagship BIOSCIENCES / Hematogenix	**NeoGenomics, Flagship, Hematogenix**: Current CRO partnerships
🤝	leap therapeutics / Leica	**Leap Tx / Leica Biosystems:** Jan 2022, CDx partners
🤝	AKOYA BIOSCIENCES	**Akoya:** Jan 2022, RNA partner (PhenoCycler-Fusion)
🚀	miRNAscope	**miRNAscope:** Nov 2020, detect small non-codingRNAs such as microRNAs
🤝	Roche	**Roche Diagnostics:** May 2019, automation partner (DISCOVERY LTRA & HT)
🤝	nanoString	**Nanostring:** Mar 2019, workflow partner (GeoMx)
🚀	BaseScope	**BaseScope:** Sep 2016, builds on RNAscope RNA ISH allowing detection of exon junction/splice variants, etc.
🧩	bio-techne	**Bio-Techne:** Jul 2016 acquisition
🤝	Leica BIOSYSTEMS	**Leica Biosystems:** Jan 2016, automation partner (BOND III & Rx)
🤝	indica labs	**Indica Labs:** Jun 2015, software partner (HALO)
🚀	RNAscope	**RNAscope:** 2011 launch, ISH kit

🤝 Partnership 🧩 M&A 🚀 Product Launch

Notes: * Competitive positioning indicates readiness for future developments in a particular area, see structure on slide 46; ** Company activity counts include only activity explicitly related to spatial biology;
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Source: DeciBio Analysis

RNAscope sees significant activity in clinical trials and has seen previous use in CDx development

Products and Services Offered		
	Name / Description	Competitive Analysis
Instruments	• No internal instrument offering	+ Compatible with standard microscope detection
Reagents*	• **RNAscope** Fluorescent Multiplex Assays: multiplex RNA-ISH* , RNA, up to 12-plex in FFPE and up to 48-plex in FF (HiPlex V2), resolution / throughput are microscope dependent, CE-IVD** • Automated assays for Leica systems and Roche Discovery platforms • Protein co-detection available (integrated and sequential IHC, Akoya PhenoCycler-Fusion) • Integration with single-cell RNA sequencing workflows (service offering)	+ Established platform technology for RNA detection, validated for clinical applications + Automation partnerships to simplify workflow / increase throughput + Multi-omic offering, sample preserved - Lower plex than other leader spatial RNA companies
Bioinformatics	• 3rd party informatics: Aperio RNA ISH Algorithm (Leica Biosystems), and HALO (Indicia Labs) for quantitative RNA-ISH analysis	+ Partnered 3rd party informatics available - No internal bioinformatics
Services	• Internal Professional assay services (PAS): E2E solutions for biomarker assay development / validation, CDx development and digital pathology IA • CRO network of CLIA-certified providers (Certified Services Provider Program)	+ Internal expertise in clinical biomarker and CDx development + Clinical trial services through a network of qualified CROs

Key Trials / Studies	Technology	Description
SHERLOC / NCT02387216: Terminated^	Comp: Jan 2019	ISH	Heregulin mRNA for patient selection in a study of MM-121 in Heregulin+ NSCLC	Ph 2	153 pts	Prospective
FORT-2 / NCT03473756: Active	Comp: Dec 2023	ISH	FGFR1/3 mRNA for patient selection in a study of rogaratinib + atezolizumab in FGFR+ UC	Ph 1	37 pts	Prospective
DisTinGuish / NCT04363801: Recruiting	Comp: Jun 2023	ISH	DKK1 mRNA for patient selection in a study of DKN-01 + Tislelizumab in G/GEJ Cancer	Ph 2	72 pts
AACR 2022 – 1723 / 20	ISH/IHC	Demonstration of integrated RNAscope ISH/IHC co-detection workflow and reagents for multi-omic TME phenotyping
AACR 2022 – 3865 / 10	ISH	Exploratory application of 12-plex RNAscope HiPlex v2 ISH assay followed by HALO IA for TME evaluation
Ferreri et al., 2021 (PMID: 33620087)	ISH	IL-6 and IL-10 mRNA assessment in PCNSL biopsies from PAMINA observational trial