Shifting the paradigm to more predictive and actionable IN MATRICO ® drug discovery
PREDICTIVE & ACTIONABLE DRUG DISCOVERY
Shifting the paradigm from *in vitro* to *in matrico*

VISION

To harness physiologically-relevant tissue-specific extracellular matrix (ECM) for more predictive and actionable drug discovery

- Lead the evolution in advanced tissue and disease models for more predictive drug discovery
- Leverage our proprietary platform technology, expertise, intellectual property, and know-how to shift the paradigm from *in vitro* to *in matrico*
- Target large markets with high unmet need, including lung and liver fibrosis (IPF and NASH), oncology (metastatic cancer), rare diseases and others
- Deliver standardized, validated assays and biomaterials that enable drug testing in human-relevant microenvironments, yielding significantly more meaningful and predictive results that increase clarity, confidence in decision-making, and likelihood for success in drug discovery
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COMPANY INTRODUCTION
COMPANY OVERVIEW

Origin
Founded in 2016
Columbia University
Laboratory for Stem Cells & Tissue Engineering

Headquarters
Brooklyn, New York

Capabilities
Tissue-Specific Biomaterials
Advanced Disease Models
Drug Testing Assay Development

Global network
12 Distributors in Territories throughout
North America, Europe, and Asia

Strategic partnerships
Pharmaceutical, Biotechnology,
Bioprinting, Microphysiologic Systems,
Non-Profit Research, Academia

Intellectual property
Patents (4 pending)
Trademarks (4 registered, 3 pending)
Trade Secrets
ACCELERATING DISCOVERY OF LIFE SAVING DRUGS

Xylyx Bio’s proprietary platform technology enables drug candidates to be tested IN MATRICO® to inform better decision making in drug discovery.

Using proprietary methods to extract tissue-specific ECMs directly from different organs, we bring the complex human disease microenvironment to drug testing workflows to accelerate the discovery of life saving drugs.
COMPANY HISTORY
De-risked by critical foundational R&D and multiple strategic partnerships

XYLYX BIO, INC.
Founded by Dr. Gordana Vunjak-Novakovic, Dr. John O’Neill and team

R&D initiated at Columbia University’s Laboratory for Stem Cells & Tissue Engineering

2010 – 2015
Validation of product concept & business opportunity

2016
$1.5M Seed 1 Financing

2017
Quality systems & manufacturing established

Advanced 3D models validation

Initial proof-of-concept revenue

2018
$4.1M Seed 2 Financing

Global distribution initiated

Disease-specific biomaterials validation

2019
$275K NIH SBIR Grant Award

Series Seed Financing Initiated

2020
$275K NIH SBIR Grant Award

2021
Compound screening validation

KEY
Corporate Milestone

Financial Milestone
## Optimized Biomanufacturing Process

| Tissue Procurement | • Established partnerships with multiple tissue procurement organizations  
|• Histopathology analyzed and confirmed within defined tissue acceptance criteria |
| Biomaterials Manufacturing | • Tissue processing protocols with In-Process Controls (IPC)  
|• Manufactured in accordance with Good Documentation Practices (GDP) |
| Quality Controls | • Biomaterials pass quality control panel of defined standards and specifications  
|• Confirmed negative for HIV-1, HBV, HCV, mycoplasma, bacteria, yeast, fungi |
LEADERSHIP & BOARD OF DIRECTORS

LEADERSHIP

Andrea Nye, MBA, MPH  
CEO & Director

John O’Neill, PhD  
CSO

DIRECTORS

Gordana Vunjak-Novakovic, PhD  
Chair, Board of Directors  
Univ. Professor, Columbia Univ.;  
Director, Lab for Stem Cells & Tissue Engineering

Anthony Curro, MBA  
Former GM, Compumedics;  
Former Director, Guidant

David King  
Managing Partner, Peak China Advisors & Peak Capital Holdings

Donna See, MBA, MPH  
CEO, Xora Innovation; Former CBO, TARA Biosystems;

Keith Greenfield  
EVP of Business Dev., AZTherapies; Co-Founder, IQuum

Matt Bacchetta, MD, MBA  
Assoc. Prof, Dept of Thoracic Surgery, Vanderbilt University Medical Center
PROBLEM: *IN VITRO MODELS ARE NOT REPRESENTATIVE*

“There are no good models for [liver fibrosis], whether they are in-vitro, in-vivo, or ex-vivo.”

Senior Scientist, Takeda Pharmaceutical

“Current approaches to both in-vitro and in-vivo are not adequate for successful target identification and validation.”

VP, Head of Molecular Signaling, Kadmon Corporation

Not representative of the human body
**SOLUTION: ADVANCED IN MATRIC® PLATFORM**

- **The cell environment matters.** Cell function is determined by biochemical and physical signals specific to cell and tissue type.

- Xylyx Bio harnesses the power of extracellular matrix (ECM), the body’s natural essential cellular microenvironment, to create biomaterials that provide cells with complex structural support and biochemical signals required for cellular function.

- By bringing the native *in-vivo* environment to the *in-vitro* setting, Xylyx Bio’s tissue-specific offerings enable cell models that are significantly more predictive of human physiology than other cell culture substrates, **accelerating scientific discoveries that benefit human life and health.**
BIOMIMETIC APPROACH

- Identify: features of human disease environment
- Isolate: the human disease environment (ECM)
- Develop: disease-specific ECM substrate
- Investigate: effects of disease ECM on human cells
- Apply: substrate in drug testing & disease models
PHYSIOLOGIC SUBSTRATES
Coating surfaces of 2D models with tissue-specific biochemical composition of the native cell microenvironment results in:

- increased cell attachment, viability, and proliferation
- enhanced function & activation of signaling pathways

Applying thick or thin gels on which to culture cells and study cell activity and function, tissue-specific 3D hydrogels provide cells with:

- a soft, physiologic substrate that is easy to use
- enhanced cell function and cell-cell interactions

Scaffolds retain the natural 3D structure, biomechanics, and topography of native tissues, allowing cells to:

- migrate, attach, and integrate to form advanced 3D constructs
- express their native phenotype, morphology, and genes
# Tissue-Specific Substrates & Data Packages

## Off-the-Shelf Products

<table>
<thead>
<tr>
<th>Source</th>
<th>Tissue</th>
<th>Format</th>
</tr>
</thead>
<tbody>
<tr>
<td>Porcine</td>
<td>Bone*</td>
<td>NativeCoat™ ECM Surface Coating</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TissueSpec® ECM Surface Coating</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TissueSpec® ECM Hydrogel</td>
</tr>
<tr>
<td></td>
<td>Cartilage</td>
<td>NativeCoat™ ECM Surface Coating</td>
</tr>
<tr>
<td></td>
<td>Heart</td>
<td>NativeCoat™ ECM Surface Coating</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TissueSpec® ECM Surface Coating</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TissueSpec® ECM Hydrogel</td>
</tr>
<tr>
<td></td>
<td>Intestine</td>
<td>NativeCoat™ ECM Surface Coating</td>
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<tr>
<td></td>
<td></td>
<td>TissueSpec® ECM Surface Coating</td>
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<tr>
<td></td>
<td></td>
<td>TissueSpec® ECM Hydrogel</td>
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<tr>
<td></td>
<td>Kidney</td>
<td>NativeCoat™ ECM Surface Coating</td>
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<tr>
<td></td>
<td></td>
<td>TissueSpec® ECM Surface Coating</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TissueSpec® ECM Hydrogel</td>
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<tr>
<td></td>
<td>Liver*</td>
<td>NativeCoat™ ECM Surface Coating</td>
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<tr>
<td></td>
<td></td>
<td>TissueSpec® ECM Surface Coating</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TissueSpec® ECM Hydrogel</td>
</tr>
<tr>
<td></td>
<td>Lung*</td>
<td>NativeCoat™ ECM Surface Coating</td>
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<tr>
<td></td>
<td></td>
<td>TissueSpec® ECM Surface Coating</td>
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<tr>
<td></td>
<td></td>
<td>TissueSpec® ECM Hydrogel</td>
</tr>
<tr>
<td></td>
<td>Skin</td>
<td>NativeCoat™ ECM Surface Coating</td>
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<tr>
<td></td>
<td></td>
<td>TissueSpec® ECM Surface Coating</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TissueSpec® ECM Hydrogel</td>
</tr>
</tbody>
</table>

*products included in IN SITE™ Metastasis Kits

## Custom Products and Data

### Source: Human

#### Format
- NativeCoat™ ECM Surface Coating
- TissueSpec® ECM Hydrogel
- TissueSpec® ECM Scaffold

#### Human: Normal

<table>
<thead>
<tr>
<th>Data Packages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Histologic Images</td>
</tr>
<tr>
<td>Histopathologic Evaluations</td>
</tr>
<tr>
<td>Biochemical Assays</td>
</tr>
<tr>
<td>Matrisome Mass Spectrometry</td>
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<tr>
<td>Other Custom Services</td>
</tr>
</tbody>
</table>

#### Human: Fibrotic/Diseased

<table>
<thead>
<tr>
<th>Data Packages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Histologic Images</td>
</tr>
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<td>Biochemical Assays</td>
</tr>
<tr>
<td>Matrisome Mass Spectrometry</td>
</tr>
<tr>
<td>Other Custom Services</td>
</tr>
</tbody>
</table>

## Additional Features

- Physiologically relevant
- Clinically predictive
- Standardized experiments
- More accurate results
XYLYX BIO PRODUCTS SUPPORT SUPERIOR CELL FUNCTION

Liver
A Low density lipoprotein uptake
B Fibrinogen secretion
C Cytochrome P450 (CYP1A2) activity
D Glycogen storage

Lung
E Airway basal cell maintenance
F
G 3D structure organization
H 3D structure size
TissueSpec® ECM Hydrogels have a unique, **tissue-specific signature**.

### TissueSpec® Liver ECM Hydrogel

<table>
<thead>
<tr>
<th>ECM components</th>
<th>Biomolecules</th>
</tr>
</thead>
<tbody>
<tr>
<td>collagens</td>
<td>type I, II, III, IV, V, VI</td>
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<tr>
<td>laminins</td>
<td>laminin γ1</td>
</tr>
<tr>
<td>glycoproteins</td>
<td>fibrillin 1, 2</td>
</tr>
<tr>
<td></td>
<td>mucin 5AC, 6</td>
</tr>
<tr>
<td>proteoglycans</td>
<td>heparin sulfate</td>
</tr>
<tr>
<td>matrix-associated</td>
<td>albumin</td>
</tr>
</tbody>
</table>

* partial list of components

### TissueSpec® Lung ECM Hydrogel

<table>
<thead>
<tr>
<th>ECM components</th>
<th>Biomolecules</th>
</tr>
</thead>
<tbody>
<tr>
<td>collagens</td>
<td>type I-VI, VIII, IX, XI, XVI</td>
</tr>
<tr>
<td>laminins</td>
<td>subunit α5, β2, γ1</td>
</tr>
<tr>
<td>elastin</td>
<td>fibrillin 1, fibulin 5</td>
</tr>
<tr>
<td>glycoproteins</td>
<td>nidogen</td>
</tr>
<tr>
<td>proteoglycans</td>
<td>heparin sulfate</td>
</tr>
<tr>
<td></td>
<td>aggrecan, hyaluronan</td>
</tr>
</tbody>
</table>

* partial list of components
TissueSpec® ECM Hydrogels demonstrate minimal lot-to-lot variability.

**TissueSpec® Liver ECM Hydrogel**

**TissueSpec® Lung ECM Hydrogel**

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**CONSISTENCY**

XYLYX BIO | 19
APPLICABLE TO MULTIPLE APPLICATIONS & TECHNOLOGIES

Applications
- Drug Development
- Cancer Research
- Stem Cell Research
- Regenerative Medicine

Technologies
- 3D Bioprinting
- Organs-on-Chips
- Bioreactors
- Microplates
EXAMPLES OF RECENT WORK WITH XYLYX SUBSTRATES

**iPSC-derived human intestinal organoids**
*Guha Lab, Albert Einstein*

**Mouse intestinal crypts**
*Wang Lab, Columbia University*

**Liver-on-a-chip**
*Nortis*

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We used tissue-specific ECM hydrogels to characterize MBC cell phenotypes and responses to drugs. These hydrogels are obtained from decellularized porcine tissue, and composition is characterized by mass spectrometry and quantitative biochemical and biophysical assays and have been shown to contain tissue characteristic extracellular matrix proteins as well as growth factors [21,22]. Scanning electron microscopy analysis of decellularized tissues revealed structural similarity and rheometry analysis showed similarities in the biophysical properties of the hydrogels to actual human tissues. Stiffness is a critical regulator of cancer cell phenotype [23]. A key consideration about the mechanical stiffness, i.e., resistance to deformation, of cell culture substrates is accounting for the enormously broad range of stiffness that is commonly applicable to in-vitro cell culture systems. Substrate stiffness typically range from quite stiff (e.g., tissue culture plastic/polystyrene: approximately 1GPa) to quite soft (e.g., hydrogels: approximately 1-10 kPa). The stiffness of most soft, healthy tissues in the human body, including liver and lung, range from 1-10 kPa [24]. The stiffness of tissue culture plastic and glass range from 1-3GPa—approximately six orders of magnitude, or one million times, stiffer than soft tissues in the human body. Notably, the modulus values of our liver and lung ECM hydrogels are within a physiologically-relevant range, especially compared to plastic. Thus, hydrogels provide an opportunity to reconstitute metastatic site environment and study drug responses and metastasis-associated phenotypes in vitro.
KEY TAKEAWAYS: ADVANCED PHYSIOLOGIC SUBSTRATES

- **Biologically Relevant:** Xylyx Bio ECM substrates contain the full milieu of proteins and growth factors present in the environment of the cell type of interest, providing the ideal conditions for maintaining cell phenotype and leading to enhanced in-vitro models and more accurate and physiologically relevant results compared to other cell culture substrates.

- **Versatile Formats:** Tissue-specific 2D NativeCoat™ ECM Surface Coatings and 3D TissueSpec® ECM Hydrogels and Scaffolds provide versatility for multiple research needs.

- **Standardized Experiments:** Substrates demonstrate consistent composition profiles across different lots for standardized experiments and reproducible results.

- **Diverse Applications:** Xylyx Bio ECM substrates enhance research across multiple fields, including drug discovery, toxicology testing, bioprinting, organ-on-a-chip, cancer research, tissue engineering, and more.
IN MATRICO® FIBROSIS ASSAYS
## LIMITATIONS OF CONVENTIONAL FIBROSIS ASSAYS

<table>
<thead>
<tr>
<th>Conventional Assays</th>
<th>Benefits</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>2D Models</strong></td>
<td>• affordable</td>
<td>• stiff, plastic substrates</td>
</tr>
<tr>
<td></td>
<td>• reproducible, rapid production</td>
<td>• lack extracellular matrix</td>
</tr>
<tr>
<td></td>
<td>• easy drug screening</td>
<td>• lack physiologic tissue structure</td>
</tr>
<tr>
<td><strong>Rodent Models</strong></td>
<td>• genetically-modifiable</td>
<td>• genetically different from humans</td>
</tr>
<tr>
<td></td>
<td>• whole organ effects</td>
<td>• non-physiologic stimuli</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• accelerated disease</td>
</tr>
<tr>
<td><strong>3D, Advanced Models</strong></td>
<td>• complex multicellular structure</td>
<td>• expensive</td>
</tr>
<tr>
<td></td>
<td>• can induce disease</td>
<td>• lack certain cell types</td>
</tr>
<tr>
<td></td>
<td>• can analyze mechanisms</td>
<td>• lack physiologic extracellular matrix</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• require optimization</td>
</tr>
</tbody>
</table>

In vitro: testing drugs ‘on plastic’ yields ~89% failure rate

- Fibrosis intrinsically involves diseased extracellular matrix (ECM).
- Compound testing systems that do not incorporate the tissue-specific fibrotic ECM lack a fundamental component that defines fibrotic disease progression, regulates cell phenotype, and affects drug response.

IN MATRICO®: next-generation drug development ‘in matrix’

- Human ECM platform that utilizes primary human cells and TissueSpec® ECM technology to conduct physiologically-relevant fibrotic disease modeling and compound testing.
- Data are consistent with clinical results observed in patients with fibrotic disease.
Xylyx Bio’s IN MATRICO® Platform utilizes extracellular matrices (ECMs) extracted directly from normal and diseased tissues to better model the human disease environment.

**Example: IN MATRICO® IPF Assay Plates**

Insets: representative trichrome staining of normal (left) and IPF (right) lung ECM scaffolds.

**IN MATRICO® Platform:**

- highly **physiologically relevant**
- recapitulates key environmental features of **human disease**
- yields **predictive results consistent with clinical data**
- **compatible** with 3D assay formats
- empowered by first-in-class **clinical data repository**
- disease areas of focus: **IPF, NASH**
- disease areas in development: **cancer**
**Products**

**TissueSpec® ECM Kits**
Human tissue-specific ECMs are available as NativeCoat™ Coatings for 2D models and TissueSpec® Hydrogels for 3D models.

**IN MATRICO® Assay Plates**
Multi-well test plates (custom) with human normal or diseased (e.g., fibrotic) ECMs are compatible with high-throughput screening.

**Services**

**Compound Testing**
IN MATRICO® Assays with diseased human liver or lung ECM for testing predictive of human disease biology.

**Lot-specific Analysis**
Data packages provide clinical context thru detailed reports on the human organ donor, tissue pathology, and matrisome.
### Unique, Differentiated, Disease-Relevant Approach

**Key Attributes**

<table>
<thead>
<tr>
<th>Fibrosis Assays</th>
<th>NASH Assays</th>
<th>NASH Assays</th>
<th>IN MATRICO® Platform</th>
</tr>
</thead>
<tbody>
<tr>
<td>procure, process human-derived, tissue-specific ECM substrates</td>
<td>+</td>
<td>+</td>
<td>++</td>
</tr>
<tr>
<td>compatible with advanced cell culture techniques</td>
<td>+</td>
<td>+</td>
<td>++</td>
</tr>
<tr>
<td>offer <em>in vitro</em> lung and liver fibrosis assays</td>
<td>+</td>
<td>+</td>
<td>++</td>
</tr>
<tr>
<td>incorporate ECM components into assays</td>
<td>+</td>
<td>+</td>
<td>++</td>
</tr>
<tr>
<td>provide clinically-relevant data packages</td>
<td>+</td>
<td>+</td>
<td>++</td>
</tr>
</tbody>
</table>
Idiopathic pulmonary fibrosis (IPF) remains high-risk for drug development because in-vitro drug testing platforms have minimal physiological relevance and fail to recapitulate the human in-vivo disease environment.

The diseased fibrotic extracellular matrix (ECM) environment is important for IPF modeling and drug testing:

(i) ECM is a fundamental lung tissue component that underlies lung function and regulates cell phenotype and gene expression.

(ii) IPF is characterized by fibrotic ECM deposition which is highly relevant in evaluating drug efficacy.

IN MATRICO® IPF ASSAY: VALUE PROPOSITION

Unlike current in-vitro assays, only IN MATRICO® IPF Assay enables drug testing in the human IPF ECM environment, yielding significantly more meaningful and predictive results that increase clarity, confidence, and likelihood for success in drug discovery.
**IN MATRICO® ASSAY CAPABILITIES**

**Cell types**
- IPF lung fibroblasts
- Normal lung fibroblasts
- Other lung cells
- Hepatic stellate cells
- Other liver cells

**ECM types**
- IPF lung ECM
- Normal lung ECM
- Fibrotic liver ECM
- Normal liver ECM

**Equipment**
- BSL2 contract services lab
- Clinical histopathology core
- Microplate reader (BioTek Synergy HTX)
- RT-qPCR system (Thermo Fisher QuantStudio 6 Flex)
- Microscopy suite (Nikon DigiSight 5.9 MP)

**Assays**
- Collagen synthesis
- Matrix remodeling
- Fibrogenic growth factors
- Custom development
Disease Relevant

The IN MATRICO® Platform utilizes human IPF lung ECM as the test substrate to induce high-fidelity fibrotic phenotype of primary lung fibroblasts. Human IPF lung ECM induces significant changes in expression of fibrosis-associated genes by primary lung fibroblasts after 48 hours. *p < 0.05

Predictive Drug Testing

The IN MATRICO® Platform predicts the efficacy of standard-of-care compounds such as Nintedanib by recapitulating the IPF disease microenvironment using human IPF lung ECM as the test substrate. By inducing the diseased phenotype of primary human lung fibroblasts, the assay demonstrates the expected significant reduction of collagen expression compared to untreated controls. Notably, response for fibroblasts treated on tissue culture plastic not consistent with clinical results observed in vivo in IPF patients.
Human Lung Tissue Procurement

- IRB-approved lung tissue procurement from nationwide tissue procurement network
- Standardized acceptance criteria for donor tissue
- Diseased tissues reviewed and confirmed by attending lung transplant pathologist

Human Lung Extracellular Matrix (ECM) Scaffolds

- Comprised of normal or IPF lung matrisome components
- Defined by structural, mechanical, and topographical features of human lung tissue
- Compatible with 48-well plate format (scaffold diameter: 8 mm, thickness: 1 mm)
- Histopathology (normal or IPF) confirmed by lung pathologist
- Negative for mycoplasma, bacteria, yeast, fungi

Human Lung Fibroblasts

- Isolated from human lung tissue and cryopreserved at passage 0
- Phenotype confirmed by immunostaining for fibronectin
- Guaranteed 15 population doublings under conditions specified by supplier
- Negative for HIV-1, HBV, HCV, mycoplasma, bacteria, yeast, fungi
- Medium contains fetal bovine serum (2%), growth supplement (1%), pen/strep (1%)

TissueSpec® Lung ECM Scaffolds in IN MATRICO® IPF Assay.
Trichrome staining of collagen fibers (blue) in fibrotic lung ECM scaffold (left) and normal lung ECM scaffold (right).

Human pulmonary fibroblasts in IN MATRICO® IPF Assay.
Immunostaining for alpha smooth muscle actin of primary normal lung fibroblasts cultured in fibrotic lung ECM scaffolds.
IN MATRICO® LOT-SPECIFIC DATA PACKAGES

First-in-class clinical data packages connect experimental results to the human disease context to enable more predictive decision-making in drug discovery.
In addition to IPF, Xylyx offers assay development opportunities across a wide range of high-impact disease areas.

- Lung
  - IPF
  - Non-small cell lung cancer
- Liver
  - NASH
  - Hepatocellular carcinoma
- Bone
  - Metastatic breast cancer
- Other disease areas
  - in Heart, Kidney, Skin
KEY TAKEAWAYS: IN MATRICO® FIBROSIS ASSAYS

• **Large Unmet Need:** Idiopathic pulmonary fibrosis (IPF) remains high-risk for drug development because *in-vitro* drug testing platforms have minimal physiological relevance and fail to recapitulate the human in-vivo disease environment.

• **ECM is Essential:** ECM is a fundamental tissue component that underlies cell function and regulates cell phenotype and gene expression. As such, fibrotic ECM is an integral component of fibrosis, and vital for modeling and drug testing.

• **Gap in Current Approaches:** Current fibrosis modeling and compound testing platforms do not incorporate native ECM, therefore lacking a defining part of the fibrotic environment.

• **Differentiated Human-Centric Approach:** IN MATRICO® Assays enable drug testing in the human ECM environment, yielding significantly more meaningful and predictive results that increase clarity, confidence, and likelihood for success in drug discovery.
IN SITE™ METASTASIS KIT
Despite advances in early detection & new therapeutic modalities, metastasis causes ~90% of cancer deaths. High mortality is due to lack of effective drugs to treat metastatic cancer.

Existing *in-vitro* metastasis models cannot recapitulate human metastatic niches and therefore yield “false, misleading, non-translatable results that retard the developmental progress needed to prevent thousands of cancer deaths every year”.

Xylyx Bio products recapitulate the physiologic cell–cell and cell–matrix interactions of the tumor microenvironment, validated by multiple external, independent collaborators and customers working in metastatic breast cancer.

Validation data prove the ability to increase predictability of cancer drug efficacy while maintaining workflow compatibility in high value drug target discovery and validation.
IN SITE™ METASTASIS KIT

• Recapitulation of site-specific microenvironments is key to identify drivers of metastasis and targets for therapeutic intervention.

• IN SITE™ Metastasis Kit contains bone, liver, and lung ECMs with tissue-specific compositions and mechanics to model colonization of tumor cells in common secondary sites.

• Mass spectrometry analysis of bone, liver, and lung ECM substrates reveals characteristic compositions highly similar to human tissue matrisomes.

IN SITE™ Metastasis Kit

Bone ECM      Liver ECM      Lung ECM
Disease Relevance
The IN MATRICO™ Platform utilizes tissue-specific bone, liver, and lung ECM substrates to induce site-specific migration of metastatic breast cancer cells which migrate significantly differently to bone, liver, and lung ECMS, consistent with clinical observations of aggressive metastatic response to lung. Cells show cancer-specific phenotype and drug response consistent with clinical results.

Predictive Drug Testing
The IN MATRICO™ Platform predicts breast cancer cell resistance to Paclitaxel (standard-of-care chemotherapeutic) by recapitulating key pathophysiological features of secondary site-specific bone, liver, and lung metastases of progesterone receptor (PR)+ breast cancer cells (T47-D). The assay demonstrates significant differences in % decrease of PR+ breast cancer cell viability across metastatic sites that cannot be captured by plastic or other conventional substrates. This result could have informed drug developers years ago that PR+ bone metastases would be highly resistant to Paclitaxel, which is observed clinically.
The ability to improve cancer drug screening holds great potential to accelerate development of safe and effective treatments, a major goal for biopharma companies working in cancer drug discovery.

The Xylyx Bio platform provides a highly physiologic, disease-relevant culture system that closely mimics the complex tissue environment, thereby enabling more predictive results.

Use of 3D tumor models with tissue-specific products is essential to identify drug targets and obtain more accurate and actionable results in early-stage drug testing.

**KEY TAKEAWAYS: IN SITE™ METASTASIS KIT**

- **Xylyx 3D Tumor Model**

  - TissueSpec®
  - Lung ECM
  - Hydrogel
  - Adenocarcinoma
  - Lung cells

  **Multi-well test plate:**
  - disease-relevant
  - reproducible
  - compatible with HTS

- **Xylyx 3D Biomaterials**
  - media
  - hydrogel

- **Competing Product 2D Plastic**
  - media

**Composition**
- Xylyx: Lung ECM
- Competing Product: Polystyrene

**Stiffness**
- Xylyx: 3 kPa (physiologic)
- Competing Product: >10⁹ kPa

**Cell to cell contact**
- Xylyx: 3D microarchitecture
- Competing Product: Only on edges

**Cell-ECM interaction**
- Xylyx: Optimal
- Competing Product: Absent
PARTNERSHIP OPPORTUNITY
### MAJOR MILESTONES & VALUE-INFLECTION

<table>
<thead>
<tr>
<th>KEY AREA</th>
<th>MILESTONE</th>
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<tbody>
<tr>
<td>Customer Discovery</td>
<td>• Validated unmet need and product-market fit with 500+ customer discovery interviews</td>
</tr>
<tr>
<td>Productization</td>
<td>• Detailed product definitions through rigorous development of underlying ECM technology</td>
</tr>
<tr>
<td>Partnerships</td>
<td>• Established nationwide network of partners to obtain corresponding high value data and close relationships with Key Opinion Leaders (KOLs)</td>
</tr>
<tr>
<td>Biomanufacturing</td>
<td>• Standardized commercial manufacturing processes &amp; quality controls</td>
</tr>
<tr>
<td>Sales &amp; Marketing</td>
<td>• Generated robust, relevant marketing materials, including standard-of-care validation datasets in peer-reviewed publications</td>
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<td></td>
<td>• Executed multiple biopharma agreements (e.g., Supplier/OEM)</td>
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<tr>
<td></td>
<td>• Initiated and expanded global distributor network to 11 worldwide distributors</td>
</tr>
<tr>
<td>Intellectual Property</td>
<td>• Robust IP portfolio, including patents, trade secrets &amp; industry-leading expertise</td>
</tr>
<tr>
<td>Revenue</td>
<td>• Proof-of-concept revenue, with corresponding pipeline of customers in big pharma</td>
</tr>
<tr>
<td>Non-Dilutive Funding</td>
<td>• Growing pipeline for grant funding, including multiple NIH SBIR Awards</td>
</tr>
</tbody>
</table>
OPPORTUNITY HIGHLIGHTS

By recapitulating the defining pathophysiologic feature of human disease, Xylyx Bio’s IN MATRICO® Platform brings much-needed insight into the efficacy of candidate compounds consistent with clinical results to accelerate decision making in compound testing.

- **Proprietary tissue-specific ECM platform** biomaterials technology developed over 10+ years, with strong intellectual property portfolio, including know-how, expertise, trade secrets and pending patents

- **Physiologic substrates and assays** support pharma workflows across multiple stages of discovery, including target validation and lead optimization, to facilitate downstream clinical translation

- **First-in-class clinical, physiological, and molecular data packages** connect experimental results to the human disease context, enabling more predictive decision-making in drug discovery

- **Collaborative partnership opportunity** in advanced tissue-specific 3D models with unique, proprietary, and differentiating ECM biomaterials
Shifting the paradigm to more predictive and actionable
IN MATRICO ® drug discovery

For more information, contact Andrea Nye, CEO, andrea@xylyxbio.com