

# Unlocking the Power of Natural Killer Cell Therapeutics

9<sup>th</sup> Sachs Immuno-Oncology Innovation Forum June 2, 2023 Waldorf Astoria, Chicago, IL

## Cytovia On Track to Become A Clinical-Stage Company



First-In-Class Flex-NK™ Bispecific Antibodies Ready to Initiate Clinical Trials in 2023,

- Addressing 2 Indications w/ Major Unmet Medical Needs & Multi-Billion Dollar Sales Potential
- GPC3-targeted FLEX-NK<sup>™</sup> Bispecific Antibody for Hepatocellular Carcinoma (HCC) & Other Solid Tumors
- CD38-targeted FLEX-NK<sup>™</sup> Bispecific Antibody for Multiple Myeloma (MM) & Other Hematological Tumors

### <u>Optimally-Designed Natural Killer Cell Products To Enhance Flex-NK™ Bispecific Antibody Therapy</u>

### Validating Data Presented at Major International Oncology Conferences in 2022 & 2023

• AACR, EHA, ESMO, SITC, ASH, ASCGT

### Ready to Scale up Revenues Through Partnerships

- First corporate partnership executed with CytoLynx, generating \$42.5 million to date, with potential future revenues of up to \$400 million
- Additional biopharma partnerships expected starting in 2023 to generate significant revenues, leveraging both technology platforms

### Strategically In-Licensing Additional Clinical-Stage Assets

Cytovia Therapeutics: An Emerging NK Therapeutics Leader



Cytovia is the first company to validate both an antibody & supporting NK cell platform, for use alone or in combination:



**FLEX-NK™ Bispecific Antibodies** to Engage Both Endogenous & iNK Cells at the Tumor Site

> TALEN® Gene-Edited iNK & CAR-iNK Cells to Enhance Flex-NK™ Antibody Therapy

- > Potential for products in both platforms to be applied either to internal pipeline or as partnered products
- Strong Technology & Product IP, with 33 owned or licensed patents
- R&D Center of Excellence in Greater Boston area, supported by world-class academic partnerships (National Cancer Institute, UCSF, New York Stem Cell Foundation, Hebrew University of Jerusalem, INSERM)
- Strategic Partnership with Cellectis (NASDAQ:CLLS) for TALEN® gene-editing

### Cytovia Pipeline Supports 2 INDs in 2023 for GPC3 and CD38 Flex-NK<sup>™</sup> Bispecific Antibodies

| Product Platform                                 | Product Candidates            | Indication | Pre-Clinical  | Clinical | IND Filings       |
|--|-------------------------------|------------|---|----------|-------------------|
| Flex-NK™<br>Bispecific<br>Antibodies             | СҮТ-303                       | НСС        | GPC3 Flex-NK <sup>TM</sup> Bispecific Antibodies                                |          | 2023              |
|  | СҮТ-338                       | MM, CTCL   | CD38 Flex-NK <sup>™</sup> Bispecific Antibodies                                 |          | Monotherapy 2023  |
| (monotherapy &<br>combination<br>with iNK cells) | CYT-103<br>(CytoLynx Program) | НСС        | GPC3 Flex-NK <sup>™</sup> Bispecific Antibodies<br>Pre-Complexed with iNK Cells |          | China IIT in 2023 |
|  | CYT-303<br>+ CYT-150          | HCC        | GPC3 Flex-NK <sup>™</sup> Bispecific<br>Antibodies + Edited iNK Cells           |          | IIT/IND 2024      |
| CAR-iNK<br>Cells                                 | CYT-503                       | HCC        | GPC3 CAR-iNK Cells  |          | IIT/IND 2024      |
|  | CYT-538                       | MM         | CD38 CAR-iNK Cells  |          | 2025              |
|  | CYT-501                       | GBM        | EGFR vIII +<br>WT CAR-iNK Cells   |          | 2025              |

HCC: Hepatocellular Carcinoma IND: Investigational New Drug IIT: Investigator-Initiated Trial GBM: Glioblastoma Multiforme



# Flex-NK<sup>™</sup> Bispecific Antibodies

# Engaging NK Cells with Cytovia's Flex-NK<sup>TM</sup> Bispecific Antibodies



**Our Proprietary Flex-NK™ Platform** 



- Worldwide patent granted
- Tetravalent format for increased affinity & avidity
- Full Fc function supports longer half-life
- Proprietary flexible linker allows simultaneous binding to 2 different cells
- Proprietary mutation ensures proper alignment of light and heavy chains and molecule stability
- Validated Manufacturability trough STC Biologics partnership

#### Engaging NK cells with NKp46



- NKp46 has significant benefits as an activating receptor
- Primary driver of NK Cell's "natural cytotoxicity"
- Shows sustained expression on NK cells in the tumor microenvironment while other activating receptors are downregulated



# CYT-303: Our GPC3-Targeted Flex-NK™ Bispecific Antibody for Hepatocellular Carcinoma

Cytovia Uniquely Positioned to Address the High Unmet Need in HCC



### HCC is The Most Frequent Form of Liver Cancer

- > Liver cancer is the 3rd leading cause of cancer-related deaths worldwide
- > HCC represents ~90% of liver cancer cases, with over 800,000 patients worldwide

### Suboptimal Therapies Are Driving High Unmet Need

- Response rate with best standard of care (Tecentriq® + Avastin®): 28%
- Average progression-free survival: 6.8 months
- > 5-year survival rate: < 9%

### Addressable Market Expected to Grow Substantially

Unresectable HCC market expected to surpass \$10 billion over the next decade

## GPC3: A Promising New Therapeutic Target for HCC and Other Solid Tumors



Glypican 3 (GPC3) is a protein expressed on the cell membrane of HCC & select other solid tumors, while predominantly absent in normal tissue. GPC3 Relative Expression in Solid Tumors



#### GPC3 Blood Levels Correlate with Severity of Disease



## Cytovia's CYT-303 Bispecific Antibody Positioned To Be First-in-Class in the Emerging GPC3 Market



(1) Athenex acquired Kuur Therapeutics in May, 2021 Source: Baumhoer et al., Am J Clin Pathol 2008;129:899-906



CYT-303 Flex-NK<sup>™</sup> Bispecific Antibody combination with Atezo +Bev checkpoint inhibitor refractory patients (2<sup>nd</sup> line immunotherapy) Rationale for CYT-303 Combination Therapy with Check Point Immunotherapy Retrospective Biomarker Analysis of Atezo + Bev First Line HCC Immunotherapy Approval

 $\langle \mathbf{Y} \rangle$ 

Since CYT-303 can activate NK cells and reduce HCC tumor burden, high GPC3 & AFP levels can be converted to low GPC3 & AFP signatures that are responsive to Atezo + Bev first-line immunotherapy



A Xu et al Nat Med 2022 and GO30140 and IMbrave150

## CYT-303 Anti-HCC Tumor Dose Response Correlates with Increased PBNK Trafficking from Blood to the Tumor





#### CYT-303

### CYT-303 Enhances HCC Tumor Killing & Reverses Dysfunction of PBNK Cells During Serial Killing



- $\rightarrow$  PBNK cells alone showed gradual reduction in serial killing of Hep3B tumors suggesting dysfunction of these cells over time
- → CYT-303 reversed dysfunction of PBNKs and enhanced serial killing of Hep3B tumors in a dose dependent manner



CYT-303 Flex-NK<sup>™</sup> Bispecific Antibody Combination with iNK cells Demonstrates Dose-Dependent Anti-Tumor Efficacy in HCC Tumor Models

> CYT-303 Tumor Growth Inhibition In a Hep3B HCC Mouse Model



Arulanandam, et al, Abstract 756, Glypican-3 (GPC3) and NKp46 directed FLEX-NK<sup>™</sup> cell engager antibody (CYT-303) distributes to tumors and shows dose-dependent tumor growth inhibition in a hepatocellular carcinoma (HCC) mouse model, Ann Oncol 2022 September: 33 (Suppl 7)

### Pre-Clinical Data Supports Advancement to IND & Clinical Trials



<u>CYT-303:</u> Cytovia's GPC3-Targeted Bispecific Antibody for Hepatocellular Carcinoma (HCC)

- Ability to Redirect NK Cells to Kill HCC Tumors Cells
- Enhances Killing Ability & Reverses Dysfunction of NK Cells
- Increased Tumor Growth Inhibition when combined with iNK Cells
- Improved Dose-Response in HCC Tumor Models in Combination with Both iNK & PBNK Cells
- No toxicity at up to 20 times expected therapeutic dose
- > Supports Weekly Administration in Patients



# CYT-338: Our CD38-Targeted Flex-NK™ Bispecific Antibody for Multiple Myeloma

Multiple Myeloma: High Unmet Medical Need Despite Significant Progress



### <u>Multiple Myeloma is the 3<sup>rd</sup> Most Common Blood Cancer Worldwide</u>

> 176,444 new cases worldwide in 2020

### Antibody & Cell Therapy Have Transformed the Market

- MM market has grown rapidly over the last 10 years with increased use of biologics and cell therapy - primarily Darzalex & CAR-Ts - to reach \$22 billion in 2021
- > J&J's Darzalex (CD38-targeted antibody) reached \$8B sales in 2022

### Addressable Market Expected to Grow Substantially with 2<sup>nd</sup> generation products

- > Darzalex moved to 1st line of treatment, opening the need for 2nd & 3rd line treatments
- > Cost, accessibility, and safety concerns limit CAR-T therapies to small number of academic centers
- Bispecific antibodies & off-the-shelf cell therapy expected to address current limitations and expand the market

### CYT-338 NK cell engager bispecific Abs are differentiated from Daratumumab Supports Monotherapy or combination with BCMA T Cell Engagers or NK Cells

|                                     | Attribute                                    | СҮТ-338   | Daratumumab |
|-------------------------------------|--|---|-------------|
| CD38 CD38<br>Fab Fab                | MOA  | CD38 cytotoxicity + NK cell<br>redirected cytotoxicity<br>(NKp46+ CD16) | ADCC        |
| Flexible Linker                     | CD38 Binding                                 | Different epitope<br>3 fold higher than Dara                            | Lower       |
| NKp46                               | NK and Macrophage<br>cytotoxicity against MM | Higher  | Lower       |
| Proprietary<br>Mutations<br>IgG1 Fc | Fractricide                                  | Minimal (unique MOA)  | Significant |
|                                     | Immune subset depletion                      | Minimal (unique MOA)  | Significant |
|                                     | Cytokine release                             | Minimal (unique MOA)  | Significant |

# Pre-Clinical Data Supports Developing CYT-338 As a Therapeutic With Differentiated Functionality Compared to Daratumumab

CYT-338 Actively Targets and Kills Multiple Myeloma Cells While Sparing Immune Cells





Favorable Safety Profile: CYT-338 also showed minimal NK cell fratricide, immune depletion, and cytokine release compared to daratumumab in human PBMCs (published data)



iNK & CAR-iNK Cells: Optimally-Designed Natural Killer Cells To Enhance Flex-NK™ Bispecific Antibody Therapy



### Cytovia Has Best-in-Class Toolbox to Develop The Next Generation of Cell Therapeutics



Induced Pluripotent Stem Cells (iPSCs)

**TALEN®** Gene-Editing

Chimeric Antigen Receptors (CARs)

## iPSC Technology: The Key To Lower-Cost, "Off-the-Shelf" Cell Manufacturing & Consistent Gene-Editing



| Donor-derived approaches are limited by:  | Advantages of iPSC-derived approach:  |
|---|---|
| Batch-to-batch variation  | Streamlined, lower-cost manufacturing with gene-editing as a one-time event   |
| Capacity bottleneck   | Consistent "off-the-shelf" product from<br>optimally-designed, single-iPSC clone (Master Cell<br>Bank)              |
| Challenging repetitive quality control needed<br>to eliminate off-target gene edits | Easier quality control supporting homogeneous<br>and consistent products, even when complex<br>gene-editing is used |



#### iNK Platform

## Augmenting the Persistence & Performance of iNK Cells Through TALEN® Gene-Editing





TALEN® Gene-Edited iNK and CAR-iNK Cells

### Gene-editing can be used to:

- Augment NK cell anti-tumor functions by targeted CAR insertion
- Ability to knock-in or knock-out specific genes involved in NK activity such as cell exhaustion, activation, tolerance, and memory

- Competitive advantages of TALEN® over other gene-editing tools:
- TALEN® demonstrates comparable knock-in and knock-out efficiency to Cas9
- TALEN® demonstrates higher target specificity with customized nucleases for specific loci compared CRISPR/Cas9

#### iNK Platform

### Improving the Cytotoxicity & Persistence of iNK Cells Through TALEN ® Gene Editing



- > In all edited iNK cells, cell killing is shown to be higher when compared to unedited iNK cells
- > Double-editing of iNK cells allows for sustained ability to kill over 3 rounds (serial killing)



# Cytovia Therapeutics Investment Considerations

## Cytovia Value Creation:

## From Vision to Operational Execution and Upcoming Clinical Milestones



#### 2019-2020 Vision & Discovery Partnerships

Leveraging Two Cutting-Edge Technology Platforms To Develop First-in-Class Immune Cell Therapeutics



#### 2020-2021 Building Capabilities

Advancing our programs through preclinical development & manufacturing

#### Cytovia Therapeutics

Miami: Finance, Clinical Development, Business Development

**Boston (R&D):** Cell Therapy & Gene Editing Center of Excellence, Pre-clinical Development

#### Partnerships

**STC (Boston):** Antibody Process Development & GMP Manufacturing

**CytoLynx (Shanghai):** R&D, GMP Manufacturing, Clinical Development

#### 2021-2022 Operational Execution

Advancing Towards a Clinical Stage Public Company

Validated Process
Development for iNK Cells,
Gene-Editing, and
Bispecific Antibodies

 Data Generation & Presentation at Major Conference

✓ IND Readiness & Clinical Trial Planning

 Audited Financials & IPO/Public Company Readiness 2023 & Beyond Clinical Milestones & Development Partnerships

2 Flex-NK™ Bispecific Antibody INDs in 2023

Finitial Clinical Data for GPC3 & CD38 programs in 2024



### **Experienced Leadership Team**









Armin Rath, PhD Chief Operating Officer

| Pfizer     | Baxter   |
|------------|----------|
| Crchimedes | SHIONOGI |



Wei Li, PhD Chief Scientific **Ófficer** 







Anna Baran-Djokovic SVP, IR & Corporate Affairs

IMMUNE Pharmaceuticals ORYZON Steba biotech Quantum / Genomics BRAIN FOR LIFE









Tony Arulanandam, PhD SVP, Pre-Clinical Research







Michael Noonan, JD, MBA Chief Financial Ófficer



Dan Chiche, MD SVP, Clinical Development & Medical Affairs



### Top KOLs in Clinical & Scientific Advisory Boards



#### Michael Caligiuri, MD

City of Hope Cancer Center Duarte, CA



#### Josep Lovett, MD, PhD

Mount Sinai Medical Center New York, NY



Yaron Ilan, MD

Hadassah Medical Center Jerusalem, IL



#### Ola Lungdren, MD, PhD

Sylvester Cancer Center University of Miami Miami, FL



Armand Bensoussan, PhD

> INSERM Paris, FR



Justin Eyquem, PhD

University of California San Francisco San Francisco, CA



#### Ofer Mendelboim, PhD

Hebrew University of Jerusalem Jerusalem, IL



## Cytovia On Track to Become A Clinical-Stage Company



First-In-Class Flex-NK™ Bispecific Antibodies Ready to Initiate Clinical Trials in 2023,

Addressing 2 Indications w/ Major Unmet Medical Needs & Multi-Billion Dollar Sales Potential

- GPC3-targeted FLEX-NK<sup>™</sup> Bispecific Antibody for Hepatocellular Carcinoma (HCC) & Other Solid Tumors
- CD38-targeted FLEX-NK<sup>™</sup> Bispecific Antibody for Multiple Myeloma (MM) & Other Hematological Tumors

### <u>Optimally-Designed Natural Killer Cell Products To Enhance Flex-NK™ Bispecific Antibody Therapy</u>

### Validating Data Presented at Major International Oncology Conferences in 2022 & 2023

• (AACR, EHA, ESMO, SITC, ASH, ASCGT)

### Ready to Scale up Revenues Through Partnerships

- First corporate partnership executed with CytoLynx, generating \$42.5 million to date, with potential future revenues of up to \$400 million
- Additional biopharma partnerships expected starting in 2023 to generate significant revenues, leveraging both technology platforms

#### Strategically In-Licensing Additional Clinical-Stage Assets