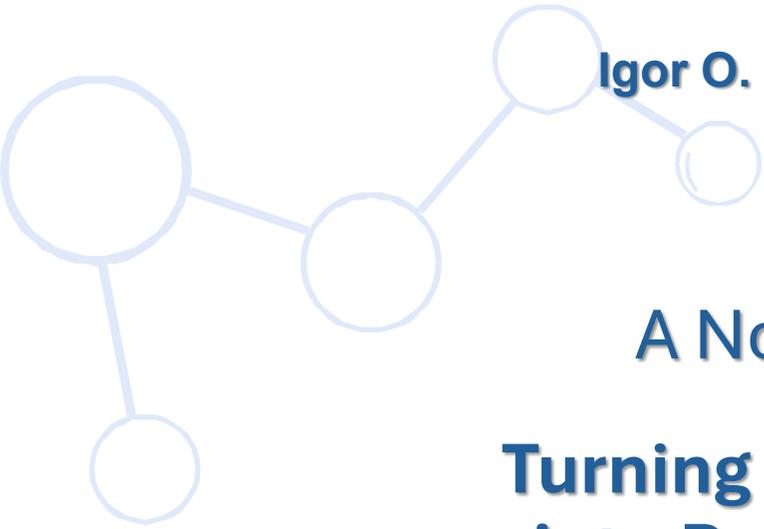




**ADVANCED
THERAPIES**
WEEK



Igor O. Nasonkin, Ph.D., CEO, Phythera Therapeutics, Inc.
<https://phytheratx.com>

A Novel Oncology Drug **MetPhyte™ PLUS**

Turning plant-derived (*Chelidonium*) molecules
into Prescription [Rx] Multi-molecular Drug



Forward Looking Statements and Confidentiality

Overview:



The statements contained herein may contain certain forward-looking statements relating to the Company that are based on the beliefs of the Company's management as well as assumptions made by and information currently available to the Company's management. These forward-looking statements are, by their nature, subject to significant risks and uncertainties. These forward-looking statements include, without limitation, statements relating to the Company's business prospects, future developments, trends and conditions in the industry and geographical markets in which the Company operates, its strategies, plans, objectives and goals, its ability to control costs, statements relating to prices, volumes, operations, margins, overall market trends, risk management and exchange rates. When used herein, the words "anticipate", "believe", "could", "estimate", "expect", "going forward", "intend", "may", "ought to", "plan", "project", "seek", "should", "will", "would" and similar expressions, as they relate to the Company or the Company's management, are intended to identify forward-looking statements. These forward-looking statements reflect the Company's views at the time such statement were made with respect to future events and are not a guarantee of future performance or developments. You are strongly cautioned that reliance on any forward-looking statements involves known and unknown risks and uncertainties. Actual results and events may differ materially from information contained in the forward-looking statements as a result of a number of factors, including any changes in the laws, rules and regulations relating to any aspects of the Company's business operations, general economic, market and business conditions, the actions and developments of the Company's competitors, and various business opportunities that the Company may or may not pursue. The Company does not intend to update or otherwise revise such forward-looking statements, whether as a result of new information, future events or otherwise. As a result of these and other risks, uncertainties and assumptions, forward-looking events and circumstances discussed herein might not occur in the way the Company expects, or at all. Accordingly, you should not place reliance on any forward-looking information or statements. All forward-looking statements herein are qualified by reference to the cautionary statements set forth in this section. The materials herein are Confidential to Phythera Therapeutics.

Executive Summary



- Phythera is developing a purified, standardized small molecule cocktail from *Chelidonium majus* as a prescription (Rx) botanical drug
Comparators: Filsuvez, Bromelain/Nexobrid, VEREGEN, Crofelemer/Mytesi, Sativex, Epidiolex
- Initial focus: inflammation (eczema) and oncology (e.g., breast, pancreatic, colorectal cancer, melanoma) and with *opportunities to diversify* and expand beyond the initial indications
- Differentiated by molecular enhancement with MDR inhibitor Tariquidar, trademark-protected (MetPhyte™ PLUS), and with ongoing further differentiation via fractionation. This is a *defined botanical drug candidate*
 - IND filing targeted within 24 months

Key Thesis

Focus: Network polypharmacology innovation in oncology



- Phytopharmaceuticals represent a largely **untapped class of therapeutics** with proven bioactivity and a strong safety record. They offer new mechanisms and drug-enhancement potential that modern oncology pipelines have yet to fully leverage.
- Strategic **combination with existing oncology drugs**—including antibody- & **CAR-T-based cell therapies**—can not only enhance efficacy and overcome resistance but also extend IP life cycles of expiring blockbuster assets.
- MetPhyte™ PLUS, our lead candidate, is a multi-molecular oncology compound composed of:
 1. A plant-derived bioactive fraction with documented clinical use and on-target anticancer activity.
 2. A small-molecule modulator of multidrug resistance (MDR) designed to sensitize tumors and restore therapeutic responsiveness.
- Phythera Tx, Inc. is seeking strategic R&D and co-development partnerships with biopharma leaders to:
 1. Evaluate synergistic potential of MetPhyte PLUS with existing oncology portfolios.
 2. Explore 505(b)(2) regulatory pathways & combination IP strategies to accelerate clinical translation & value creation

Strategic Thesis



Phythera Therapeutics, Inc: <https://phytheratx.com>, a C-corp Delaware company with R&D in California



IGOR O. NASONKIN PHD
CEO/Co-Founder



CHARLES IRVING PHD
CDO/Co-founder



EDINAL BSECE, CS
COO



OSCAR CUZZANI MD
Clinical Advisor



SERGEY B. LUSHPA MD
Advisor, Botanical oncology



JUDITH SEGALL, MS
Corporate Secretary

- Phytopharmaceuticals: a validated yet underexploited therapeutic class with unique mechanisms of action and clinical safety record.
- Opportunity to enhance efficacy and extend IP protection for existing oncology drugs — including antibody and CAR-T-based therapies.
- **Potential to re-sensitize resistant tumors via MDR modulation.**

Lead Candidate: MetPhyte™ PLUS



A multi-molecular oncology compound composed of:

1. Plant-derived bioactive small molecules – with documented clinical use and on-target anticancer properties
2. Small-molecule MDR modulator – restores sensitivity to existing treatments and amplifies therapeutic response.

Mechanism: Combats drug resistance and enhances synergy in solid and ocular tumors.

Partnership Opportunity



Phythera **seeks strategic co-development partners** to:

- Evaluate synergy with existing oncology assets (antibody, cell, and gene therapies).
- Pursue accelerated 505(b)(2) clinical/regulatory pathways.
- Explore combination IP and lifecycle management strategies for expiring blockbuster drugs.

Why Partner with Phythera



- Novel yet de-risked mechanism – leveraging known bioactives.
- Translational potential demonstrated in patient-use settings abroad.
- Regulatory flexibility via 505(b)(2) pathway.
- Low-cost, high-impact innovation aligning with pharma lifecycle management goals.

Thank you

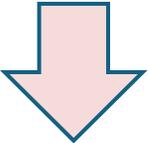


- **Join us** in redefining novel plant-inspired medicine for oncology and inflammatory diseases
- Seeking strategic partners, co-investors, and pre-IND collaborations
- Contact: **Igor Nasonkin**
Inasonkin@phytheratx.com
- **Charles Irving**
Cirving@phytheratx.com

Thank you /extra slides 

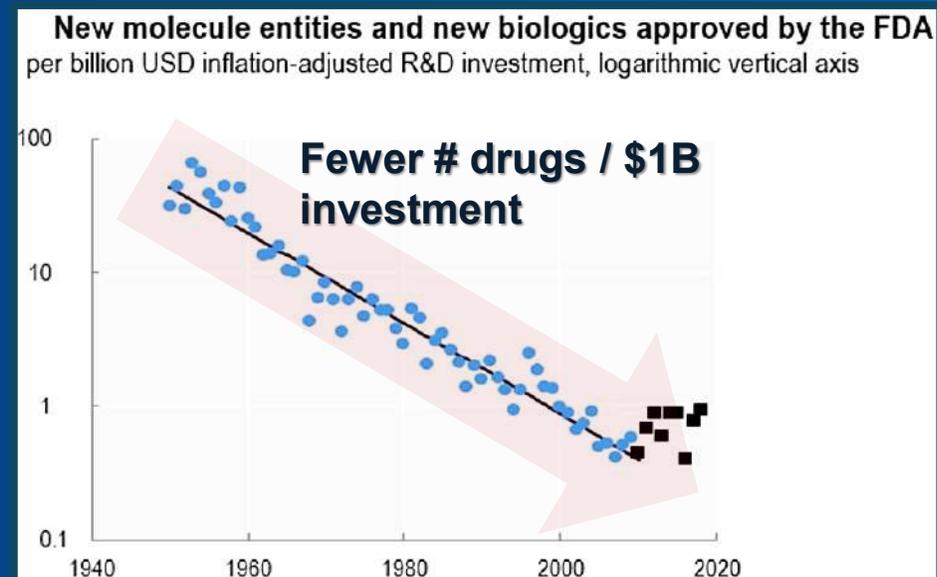
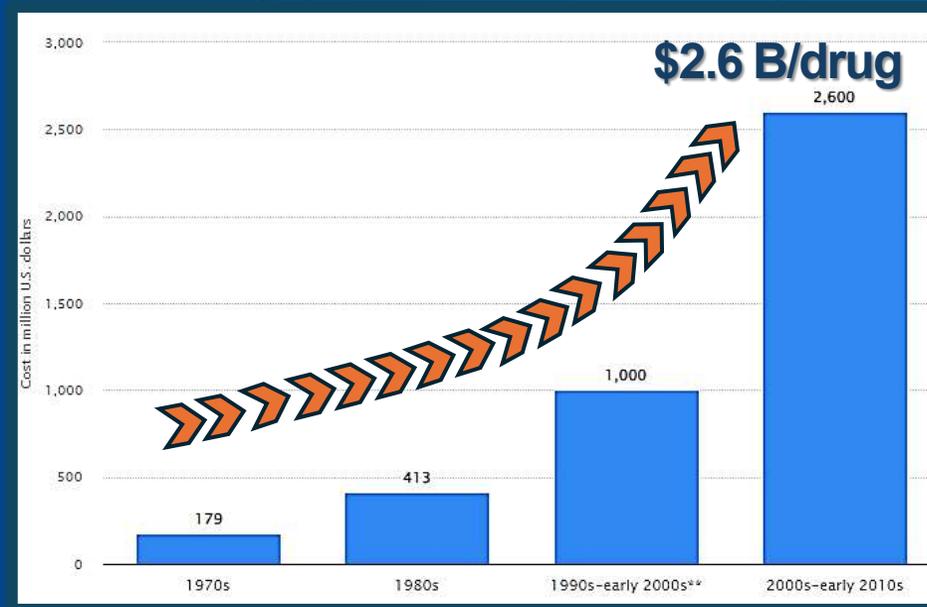
PROBLEM

For investors:

- Drug development is a **costly** process:
only **3.4-5%** of the drugs, which enter clinical trials
(in oncology) received **FDA approval** in the past 20 years
- **Declining R&D productivity** of Big Pharma:
The **exhaustion** of opportunities for pharma **innovation**
& “**patent cliff**”

- Fewer “Unicorn” biotechnology companies (startups with
≥ \$1B valuation) with 100:1 or higher ROI

How to de-risk your investment?

Rising cost of developing a drug in the U.S. from the 1970s until today (in million U.S. dollars)



PROBLEM

For investors and patients:

IMPRECISION MEDICINE

For every person they do help (blue), the ten highest-grossing drugs in the United States fail to improve the conditions of between 3 and 24 people (red).

1. ABILIFY (aripiprazole)
Schizophrenia



2. NEXIUM (esomeprazole)
Heartburn



3. HUMIRA (adalimumab)
Arthritis



4. CRESTOR (rosuvastatin)
High cholesterol



5. CYMBALTA (duloxetine)
Depression



6. ADVAIR DISKUS (fluticasone propionate)
Asthma



7. ENBREL (etanercept)
Psoriasis



8. REMICADE (infliximab)
Crohn's disease



9. COPAXONE (glatiramer acetate)
Multiple sclerosis



10. NEULASTA (pegfilgrastim)
Neutropenia



Based on published number needed to treat (NNT) figures. For a full list of references, see Supplementary Information at go.nature.com/4ck7BE.

- IMPRESION MEDICINE:

For every person these (major blockbuster) drugs help (blue), these 10 highest-grossing drugs in the United States fail to improve the conditions of between **3 and 24 people**

(red):

e.g. they **work in 25% to 4% of patients**

Defending Against Tough Diseases

Multi-molecular drugs for Multifactorial Diseases like cancer, inflammation

Combination Therapies

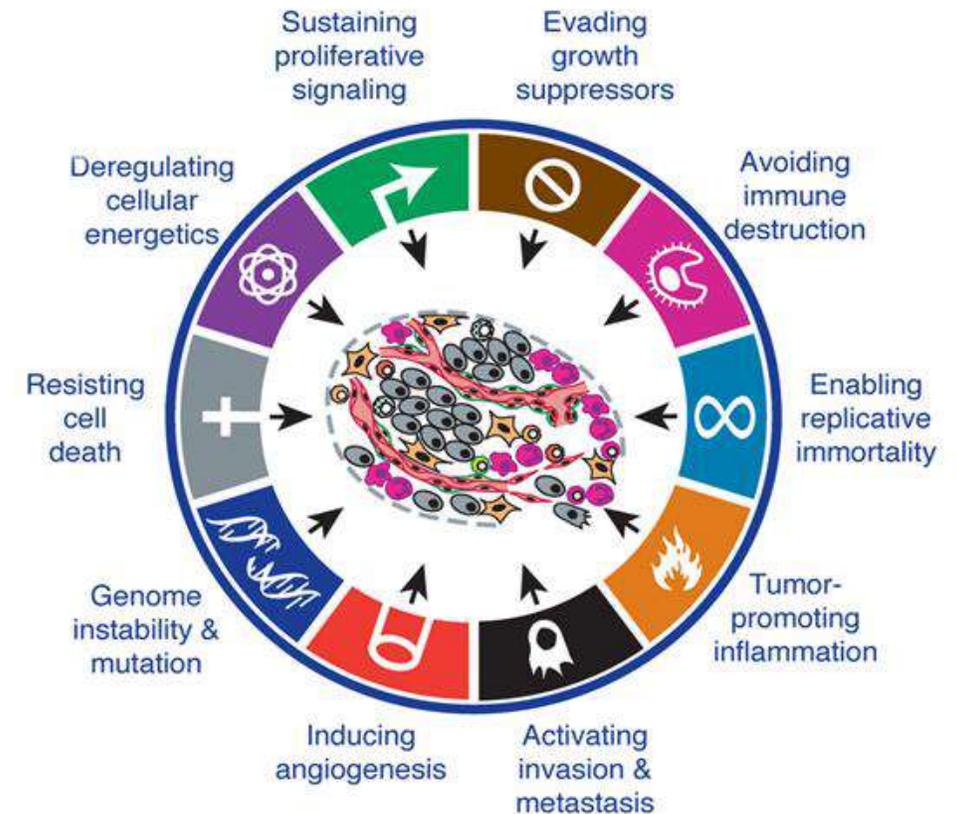
- Attack multiple pathways
- Minimize drug resistance
- Cancer, tuberculosis, leprosy, malaria
- HIV/AIDS (standard 3 drug cocktail)

- Example of **3-drug cocktail chemo (EAD)**:
Doxorubicin, all-trans-Retinoic Acid, entinostat

Critical Cancer Pathways:

- Traditional drugs generally impact one pathway
- **Multi-molecular drugs** like MetPhyte™ can affect many

**Hallmarks of Cancer Pathways –
suppressing one is not sufficient to treat cancer**



*Hallmarks of Cancer: The Next Generation
Douglas Hanahan and Robert A. Weinberg. Cell 2011,
vol.144 issue 5, p646-74*

The Problem

- Many botanical agents with therapeutic potential are unfit for Rx use due to toxicity and lack of standardization
- *Chelidonium majus* has shown potent anticancer and anti-inflammatory activity and standardization approach (CMC control) has been worked out by Phythera, but the *plant has been viewed as a nutraceutical*
- There are No FDA-approved botanical drug products for cancer/inflammation despite broad traditional use (topical and **oral**)

The Opportunity

- First-in-class botanical oncology/inflammation *multi-molecular* drug with Rx-grade safety profile and promising safety/efficacy data in patients (abroad)
- Converted to Rx drug candidate due to *molecular enhancement* by Tariquidar
- Huge unmet need for safe & gentle drugs in niche cancers (e.g., pancreatic, colorectal/GI, breast, lung, skin) and chronic inflammation
- Botanical drug pathway allows broad IP protection without single-compound isolation, while botanical enhancement creates a *platform technology*

Our Solution & Mechanism of Action

- **Multiple pathways** of anticancer action in **ONE drug**:
 - Induces apoptosis in cancer cells (via PKC and mitochondrial pathways)
 - Suppresses angiogenesis and cancer cell proliferation
 - Immunomodulatory effects
- Early *in vitro* and *in vivo* models show strong activity against colon, breast, skin, brain, lung, and other cancers
- Molecular enhancement increases drug's **efficacy** and **bioavailability** in cancer cells

- Maintains **multi-component natural synergy** per FDA botanical drug guidance
- Phythera is developing proprietary multi-step process to further define this botanical:
 - Fractionation to isolate bioactive alkaloid-rich components
 - Removal of potentially toxic components (e.g., lectins, latex enzymes, phenolic acids)
 - Stabilization and standardization using GMP and HPLC fingerprinting

Regulatory Strategy

- FDA Botanical Drug Development Pathway: **505(b)1 or 505(b)(2)**
 - IND planned: 24 months
 - Phase 1: safety/tolerability in patients with advanced cancer
 - Phase 2: efficacy in selected cancer indications (orphan drug potential)
- Select **one orphan drug** designation for FDA pathway (pancreatic, retinoblastoma, GBM, sarcomas, uveal melanoma cancers), which are **rare, aggressive** and lack of effective and satisfactory standard therapies = urgent & unmet needs, and 1-2 backup indications

Competitive Landscape & Intellectual Property

Competitive Landscape

- No FDA-approved *Chelidonium*-based drugs but 2 previous attempts (Amytosin, Ukrain)
- No multi-molecular Rx botanicals for oncology/inflammation
- **Filsuvez**, **Bromelain/Nexobrid**, **VEREGEN**, **Crofelemer/Mytesi**, **Sativex** are precedents; also **Acthar**
- Differentiated by dual-action potential (oncology + immune cells)

Intellectual Property

- **Composition of matter** patent (*molecular enhancement*)
- US 2024/0131105 A1, pending
- Use patents (anticancer, anti-inflammatory –work in progress)
- Manufacturing/process IP (detoxification, fractionation, formulation –work in progress)

Business Model & Exit

- Licensing to mid-size biotech or pharma after Phase 1-2
- Co-development opportunities with oncology or/and inflammation players
- Strategic exit post proof-of-concept: est. \$100–300M valuation potential
- **Large oncology market** (close to \$200B USD) and rapidly growing – our multi-molecular drug could be repurposed for other oncology indications

Financials & Use of Funds

- Preclinical and IND-enabling studies: \$4M
- Phase 1 clinical trial: \$5–7M (potentially less)
- IP, regulatory, and CMC development: \$2M
- **Total raise: \$10–15M**

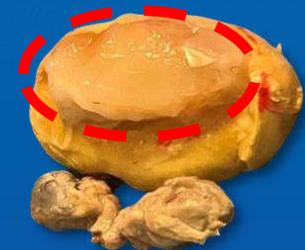
Success to Date

MetPhyte™ Plus: Enhanced botanical drug

- Modulates cell cycle, killing and suppressing growth of human cancer cells
- Has **20+ bioactive small molecules**: alkaloids, terpenoids etc.
- Impacts wide range of cancer-associated pathways & functions
- Inhibits cell migration

MetPhyte™ Plus kills tumor cells *in vivo*

(In a chick embryo implanted with human cancer cells)



No treatment:
Tumor grows & blocks embryo development



MetPhyte™ Plus:
Tumor cells destroyed & embryo develop normally

Cancer	Type	MetPhyte™	MetPhyte™ Plus
Mammary Adenocarcinoma	CRL2351 AU565 ATCC	✓	✓✓✓
Osteosarcoma	CRL1543 AU565	✓	✓✓✓
Melanoma	SK-MEL-2 HTB-68 ATCC	✓	pending
Melanoma	SK-MEL-1 Addex Bio	✓	✓✓
Melanoma	A375 Addex Bio	✓	✓✓
Neuroblastoma	CRL2149 SK-N-DZ ATCC	✗	✓✓
Retinoblastoma	Y-79 Addex Bio	✗	✓

Kills Cancer Cells

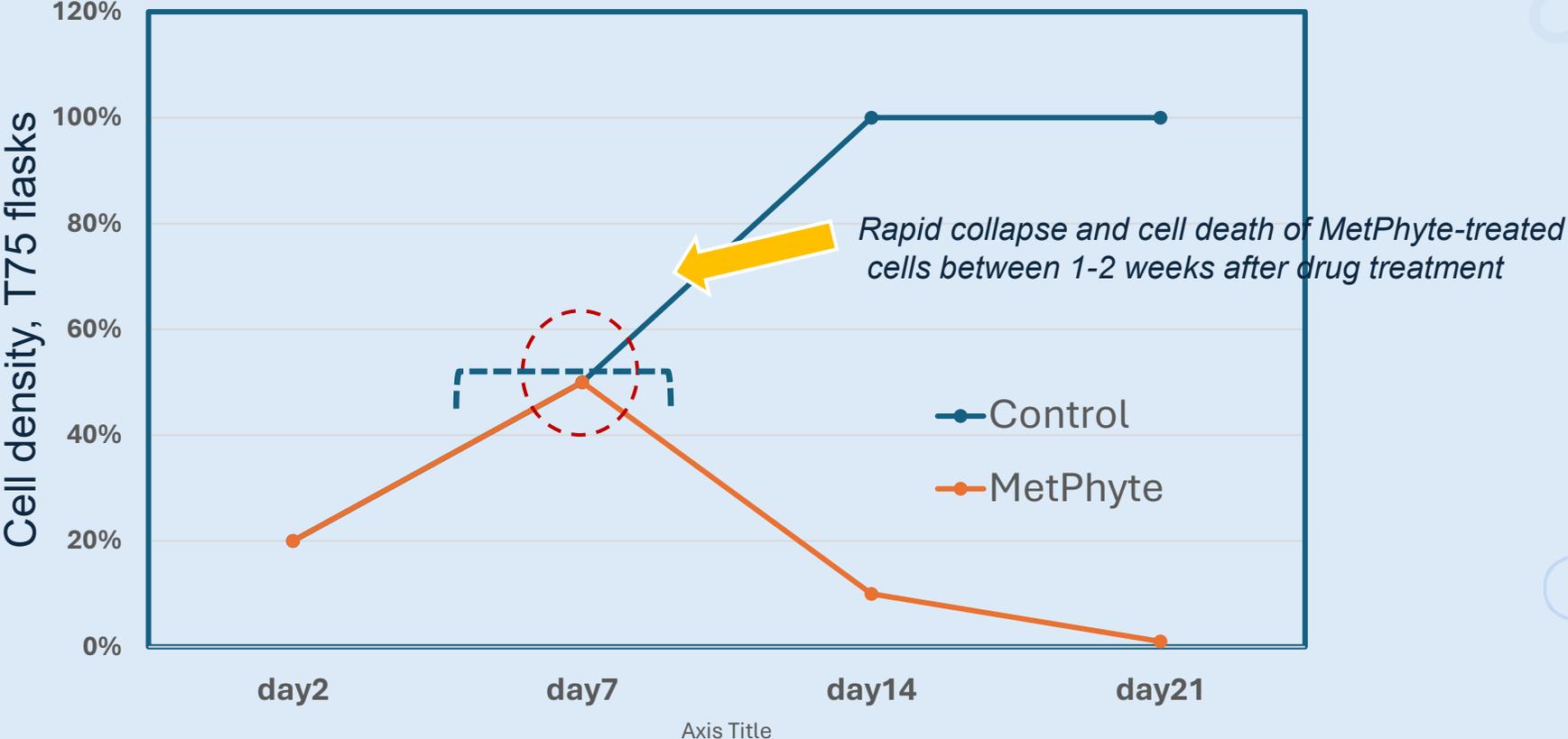
Healthy Cells	Type	Cells Killed	Cells Killed
Foreskin, primary	Foreskin fibroblasts X-Gene	✗	✗
Adult fibroblasts, primary	PC-1 Adult fibroblasts BioTime	✗	✗

Spares Healthy Cells

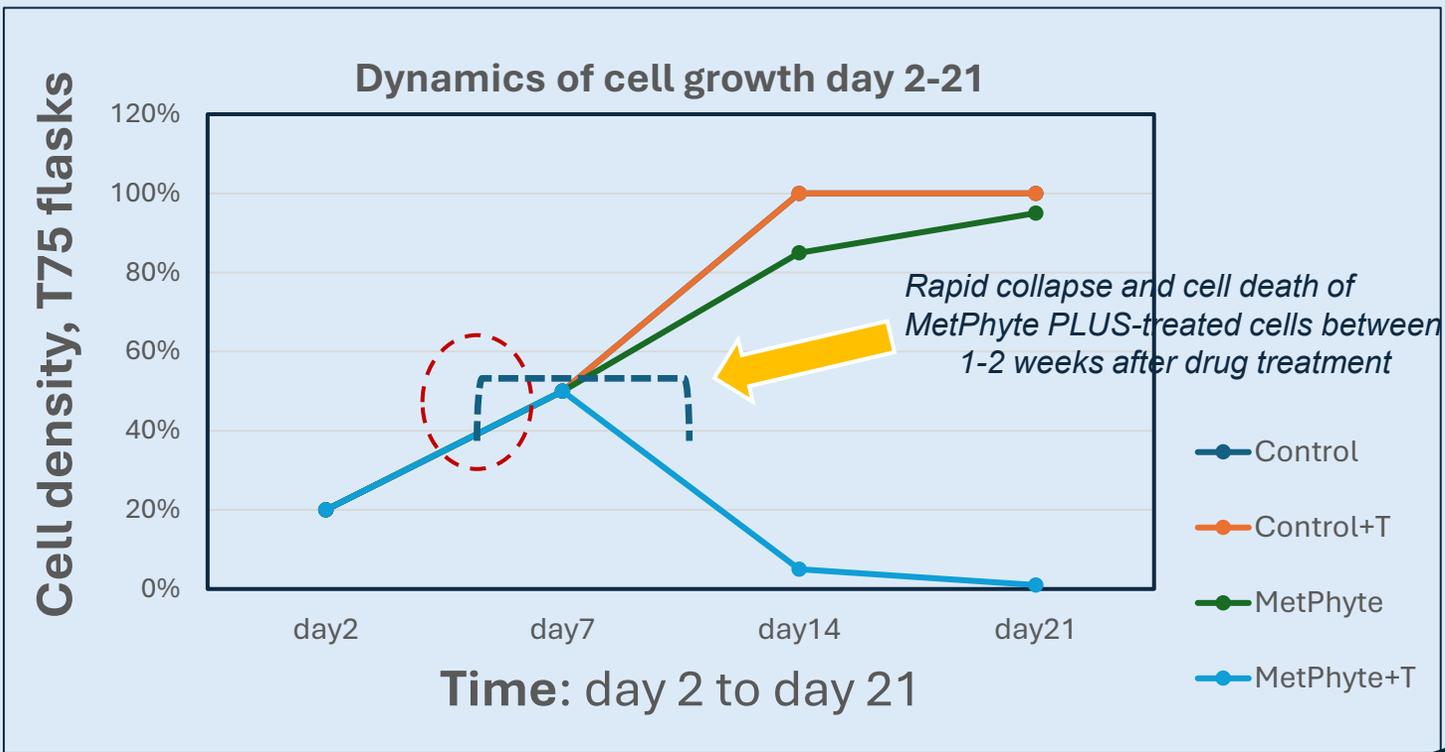
◆Multi-molecular ◆Cell data ◆In ovo data
◆Molecular (RNA-Seq) data

- Quick summary of the experiments & plots : **cell death curves**, LD50, in ovo data

Dynamics of cell growth, human embryonic carcinoma cells n2102Ep, Day 2-21, treated with MetPhyte™ or Control



**Testing MetPhyte (MP)TM PLUS
A375 human malignant melanoma model**

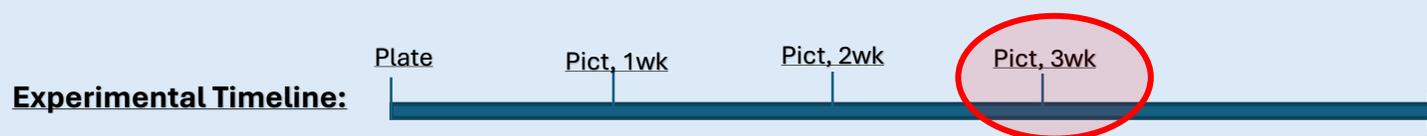


3 weeks of treatment

Design

Drug: MetPhyte, MetPhyte PLUS

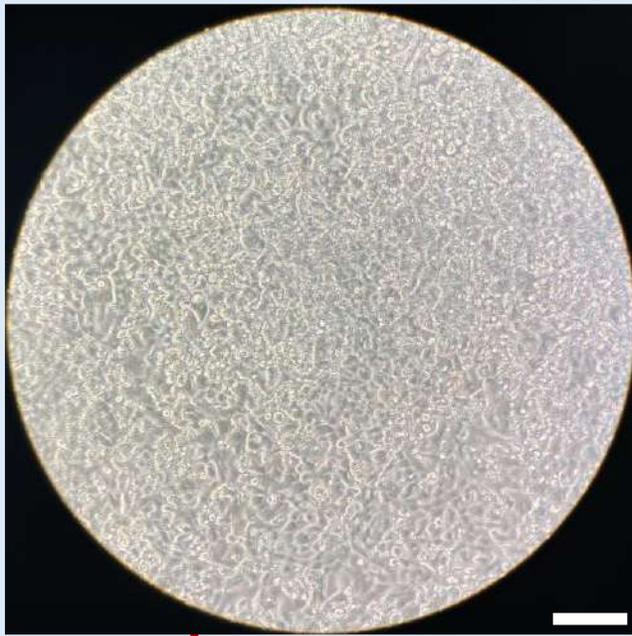
Control Extraction media (Control); Extraction media +T (the enhancer) = Control + T



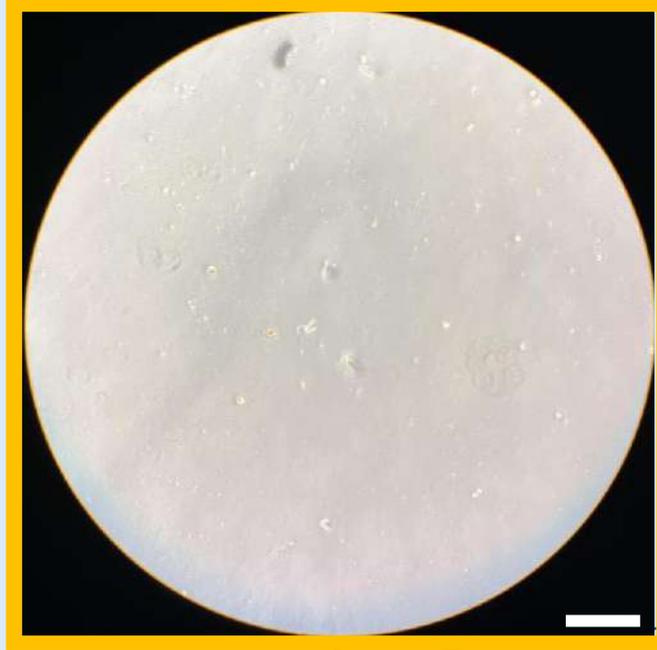
3 week of treatment

100 ul MP
in 10ml media

1



2

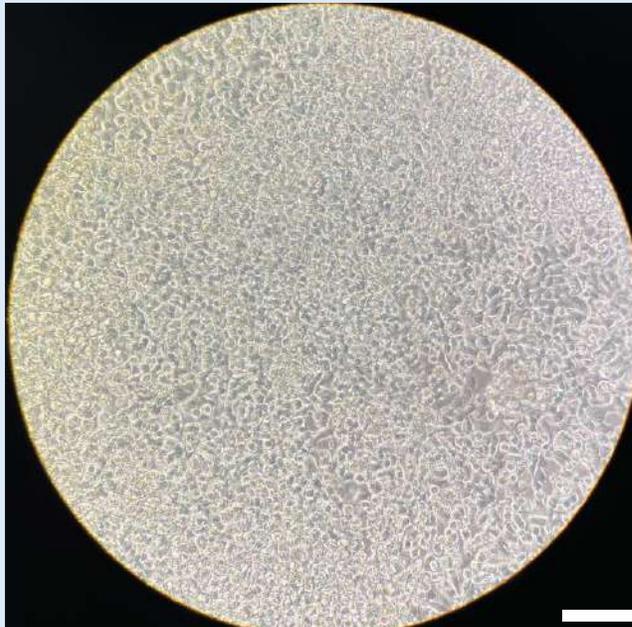


100 ul MP
in 10ml media +T

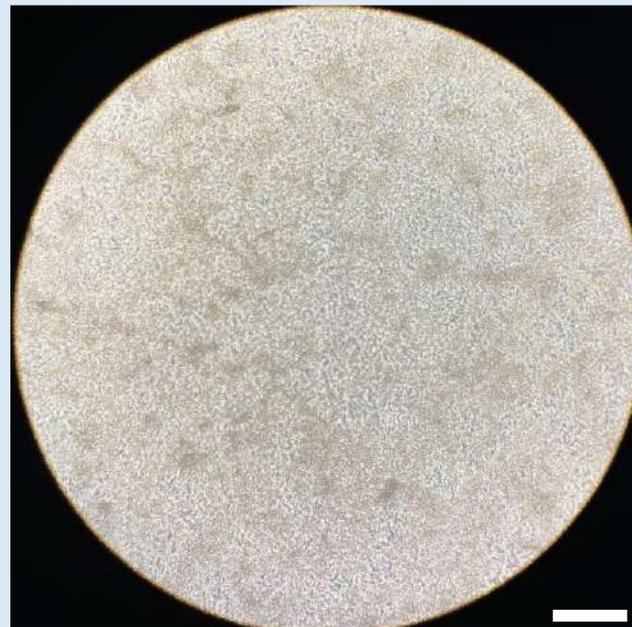
1,3 and 4
identical

100 ul CONTROL
in 10ml media

3



4



100 ul CONTROL
in 10ml media +T

Difference between 2 & [1,3,4] after 21 days:

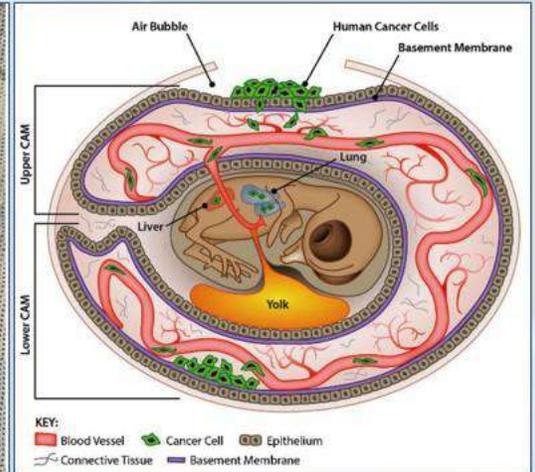
50 μm

• Quick summary of the experiments & plots : cell death curves, LD50, **in ovo data**

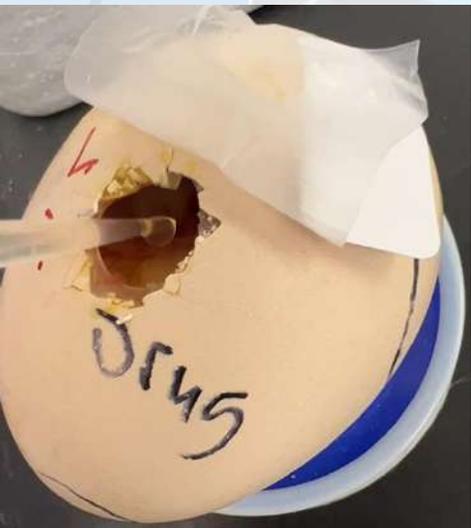
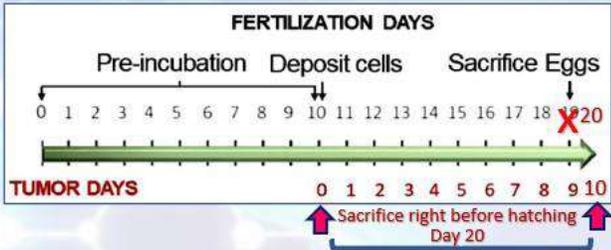
10-day CAM (Chick Chorioallantoic Membrane) assay to demonstrate the efficacy of MetPhyte™ PLUS to suppress the growth of human met. cancer cells (neuroblastoma)

Control
(media used for MetPhyte™ extraction):
RESULT: Cancer cells grew vigorously, formed a mass of cells (dotted circle) and block chick embryo development

MetPhyte™ PLUS -treated
RESULT: Cancer cells growth was suppressed by treatment with MetPhyte™ PLUS. As a result, chick embryos formed normally in "treated" group. This can also be used as an indirect indication of **lack of toxicity** of MetPhyte™ PLUS



Translational Oncology Vol.6, #3, 2013 pp273-281



1. Cancer cell grafting on CAM, day 10 embryo development (day 0 of the experiment)
2. Monitoring the chick embryos @ days 14-16)
3. Monitoring the chick embryos @ days 19-20): The embryos are fully formed in "treated" group

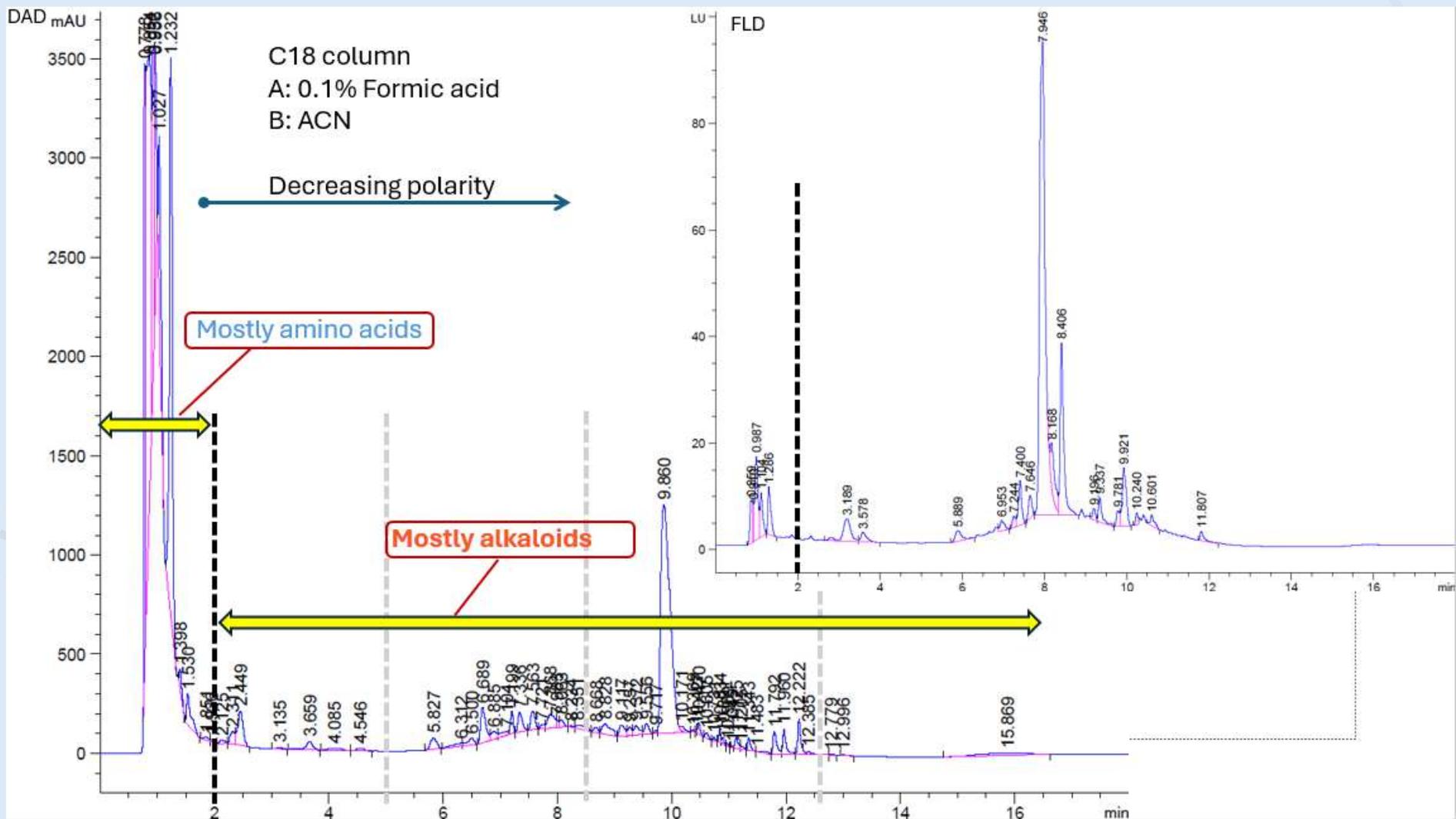


Deposited (on CAM) human (neuroblastoma) cancer cells developed for 10 days



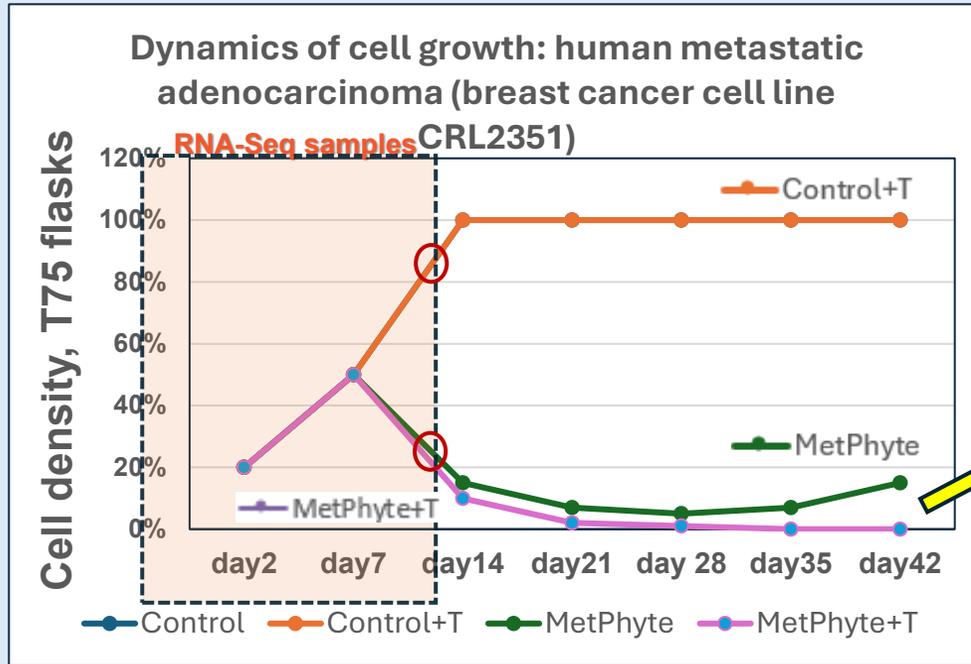
Proprietary and Confidential

LC-MS data, MetPhyte prep. from Central Asia



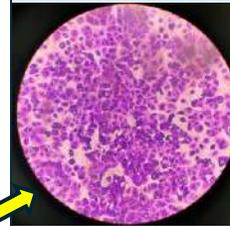
In collaboration with Dr. Doudareva, Purdue University

• **RNA-Seq bioinformatics** data, human metastatic breast cancer cell model CRL2351

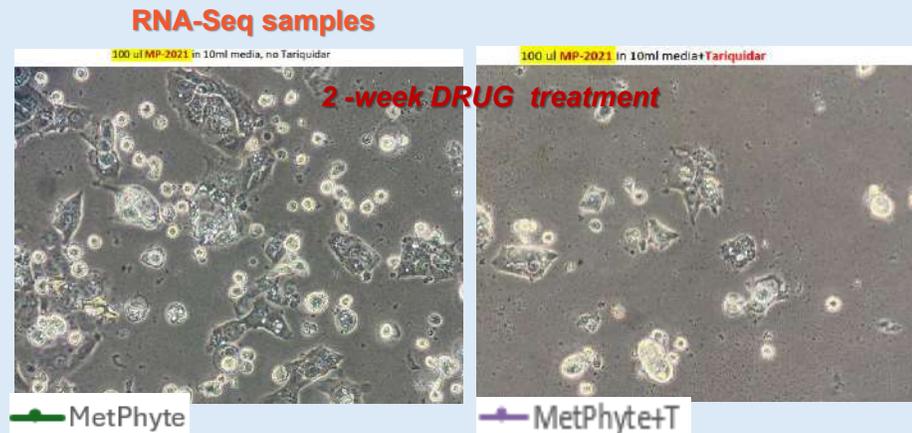


Mechanism of Action knowledge / description is NOT required for a drug approval by FDA

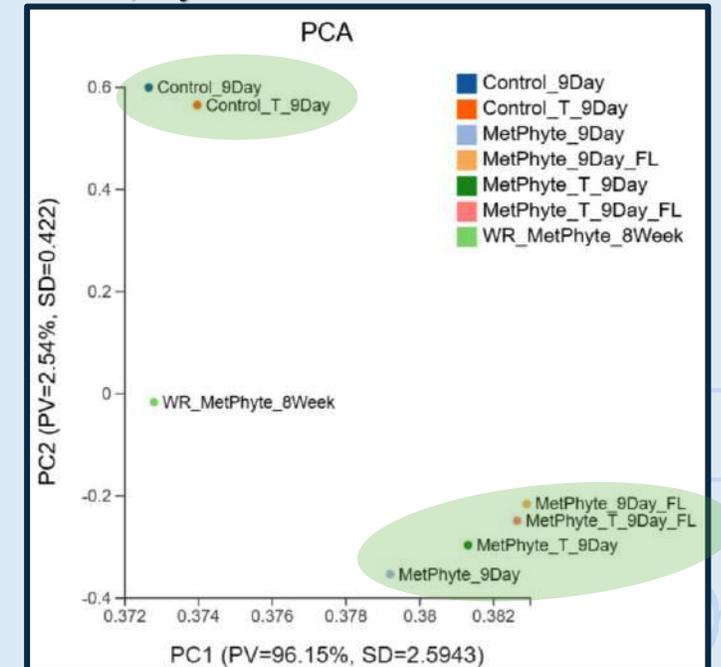
Colonies slowly growing, wk 5-6+



100% cell death wk 5-6+

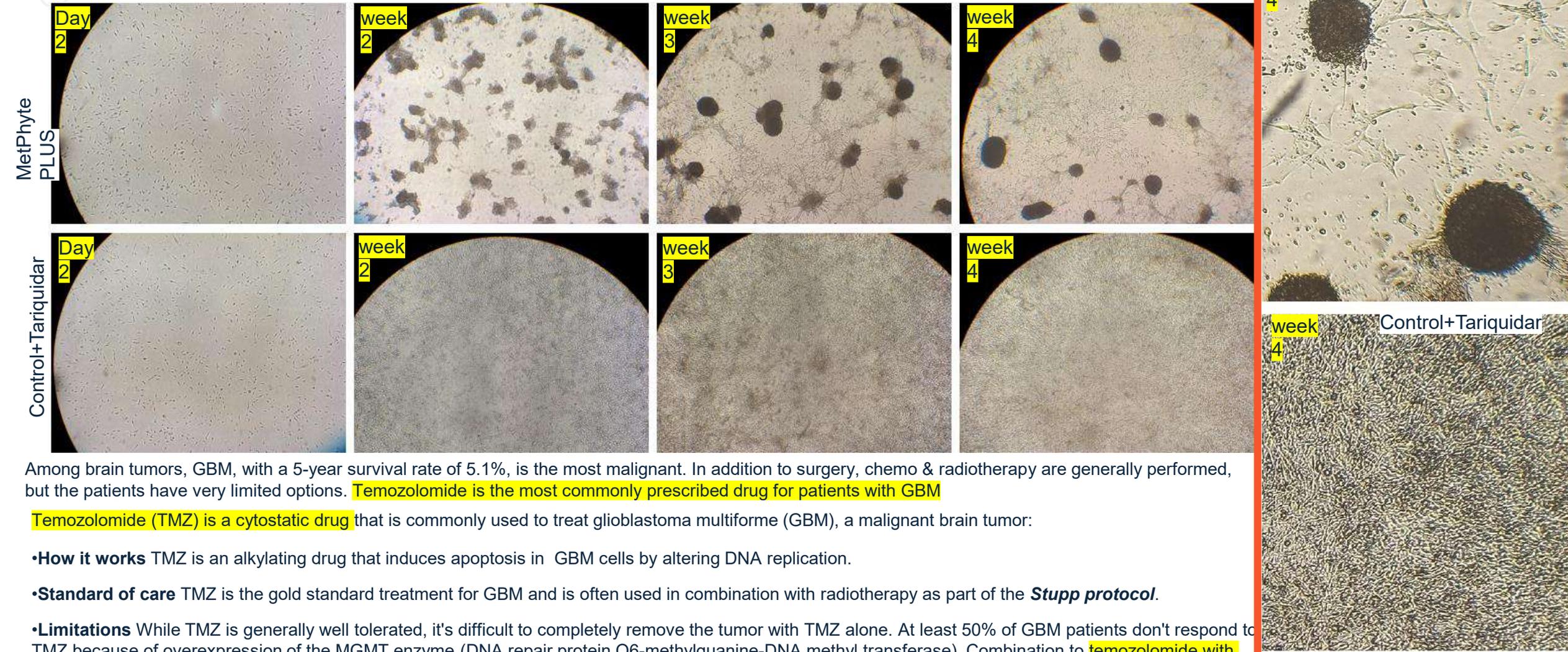


Principal Component Analysis (PCA) plot, the latest timepoint available, day 9.5: bid difference DRUG vs CONTROL



Summary of ongoing glioblastoma experiments (MetPhyte PLUS for GBM treatment)

Cytostatic effect of MetPhyte PLUS in GBM human cell model (U87MG line)



Among brain tumors, GBM, with a 5-year survival rate of 5.1%, is the most malignant. In addition to surgery, chemo & radiotherapy are generally performed, but the patients have very limited options. **Temozolomide is the most commonly prescribed drug for patients with GBM**

Temozolomide (TMZ) is a cytostatic drug that is commonly used to treat glioblastoma multiforme (GBM), a malignant brain tumor:

- How it works** TMZ is an alkylating drug that induces apoptosis in GBM cells by altering DNA replication.

- Standard of care** TMZ is the gold standard treatment for GBM and is often used in combination with radiotherapy as part of the **Stupp protocol**.

- Limitations** While TMZ is generally well tolerated, it's difficult to completely remove the tumor with TMZ alone. At least 50% of GBM patients don't respond to TMZ because of overexpression of the MGMT enzyme (DNA repair protein O6-methylguanine-DNA methyl transferase). Combination to **temozolomide with other anticancer agents** have been investigated.

Could MetPhyte PLUS be a better alternative than TMZ for GBM treatment or work in combination with TMZ to improve treatment outcomes?