Cloaked Therapeutics, LLC

Using the Body's Own Mechanisms To Transform Chemotherapy

TumorSelect® Technology
TumorSelect® Paclitaxel

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- **TumorSelect® is a Chemotherapeutic drug delivery technology**
  - **Targets tumors**
  - **More effective tumor kill**
  - **Will greatly reduce toxic side effects**
- **Very solid intellectual property protection**
  - **Drug substance and drug product**
    - **Issued US patents**
    - **Issued foreign patents**

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The Problem

- **The American Cancer Society estimates almost 2,000,000 new US cancer cases in 2021**
- **Over 600,000 US cancer deaths in 2021 (Between March 2020 and now roughly 600,000 deaths from Covid-19)**
- **Cancer chemotherapy is barbaric**
- **Cancer chemotherapy is inadequately selective**

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Development Options

- **Discover and develop a new drug**
  - **High risk**
  - **10-12 years and $650 million**
- **TumorSelect® paclitaxel**
  - **Identify and develop a new delivery strategy**
    - LDL as a delivery mechanism
  - **Selectively delivered to tumors**
  - **By choosing a well known clinically utilized drug (paclitaxel)we reduce risk of development failure**

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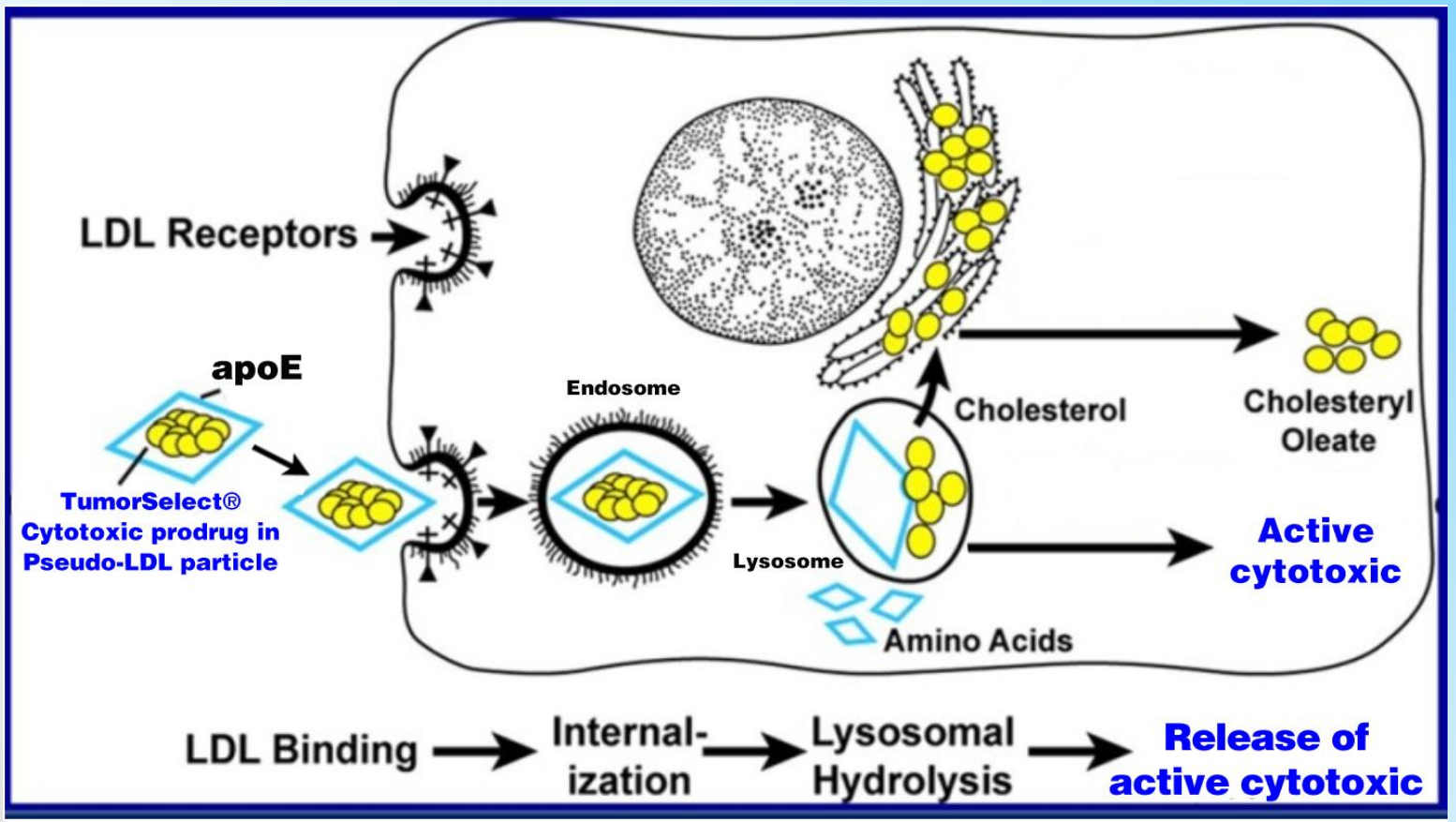
TumorSelect® LDL Mechanism



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Four Questions to Be Addressed

1. **Can a pseudo-LDL nanoparticle be created which is sufficiently similar to natural human LDL particles to be physiologically recognizable and stable enough to serve as a delivery vehicle for a cytotoxic payload?**

2. **Can a suitable paclitaxel derivative be prepared to be efficiently incorporated into and retained in the delivery formulation?**

3. **Does the proposed TumorSelect® construct of cytotoxic derivative and delivery vehicle improve TI of the cytotoxic and still retain efficacy?**

4. **Does the TumorSelect® technology selectively deliver cytotoxic to tumor tissue as proposed?**

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Can We Make Suitable Pseudo-LDL Particles?

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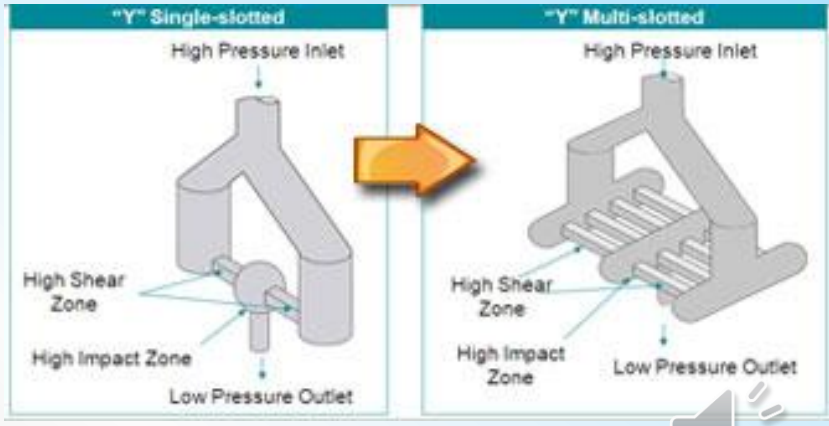
Pseudo-LDL Particles

- **Manufacturing**
  - **MicroFluidizer®**
    - Process coarse emulsion
    - Recirculating continuous flow
    - Reduces particle size into desired range
    - Has been scaled up by others to GMP-approved commercial scale
  - **Rational development of processing conditions**
    - Buffer composition
    - Total solids content and composition
    - Interaction-chamber geometry
    - Temperatures
    - Pressure



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A Suitable Lipophilic Derivative of Paclitaxel to incorporate and be retained in the pseudo-LDL nanoparticle

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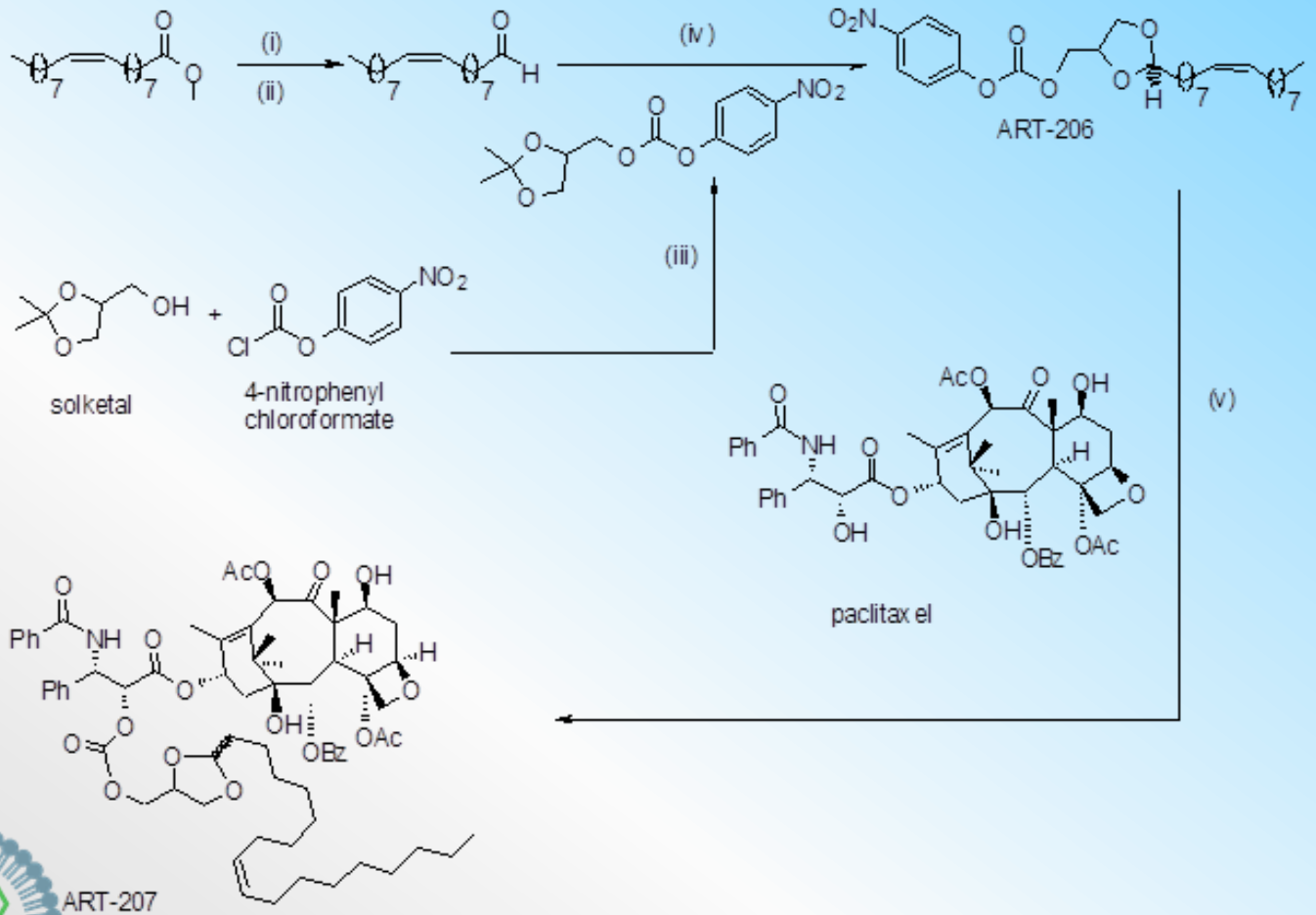
A Suitable Derivative to Incorporate



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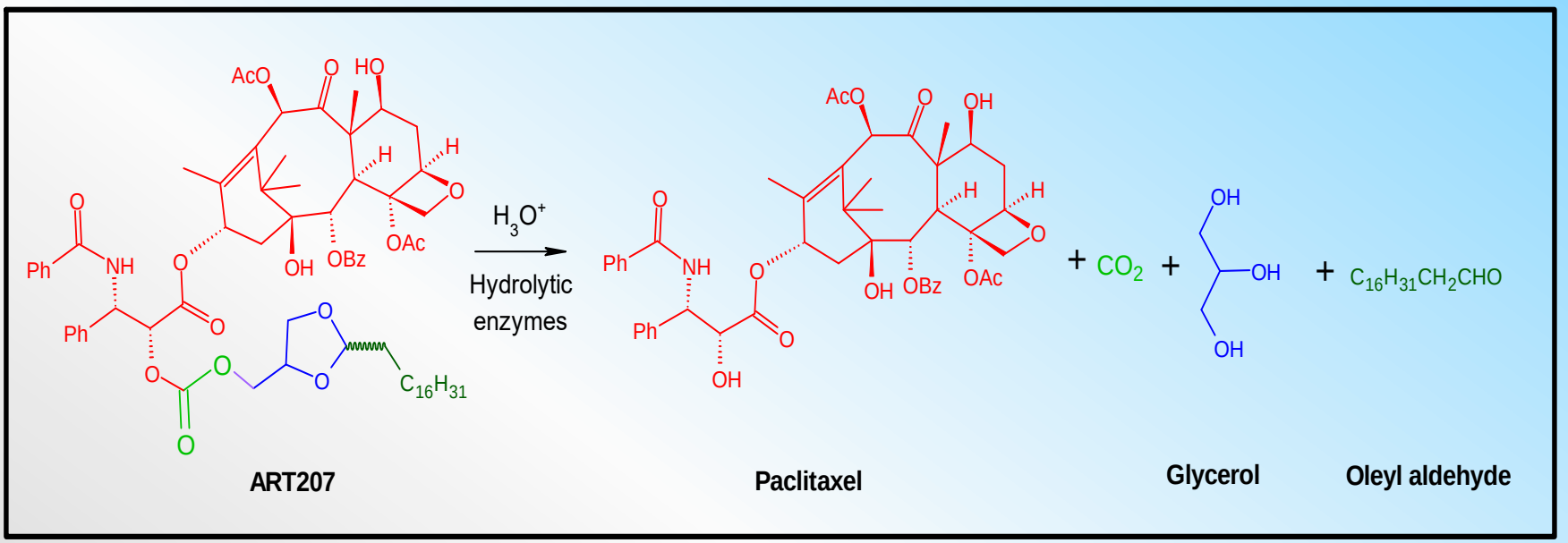
TumorSelect® Paclitaxel Lysosomal Release



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Does the Construct of the Cytotoxic Drug and Delivery Formulation Retain Efficacy and Improve TI?

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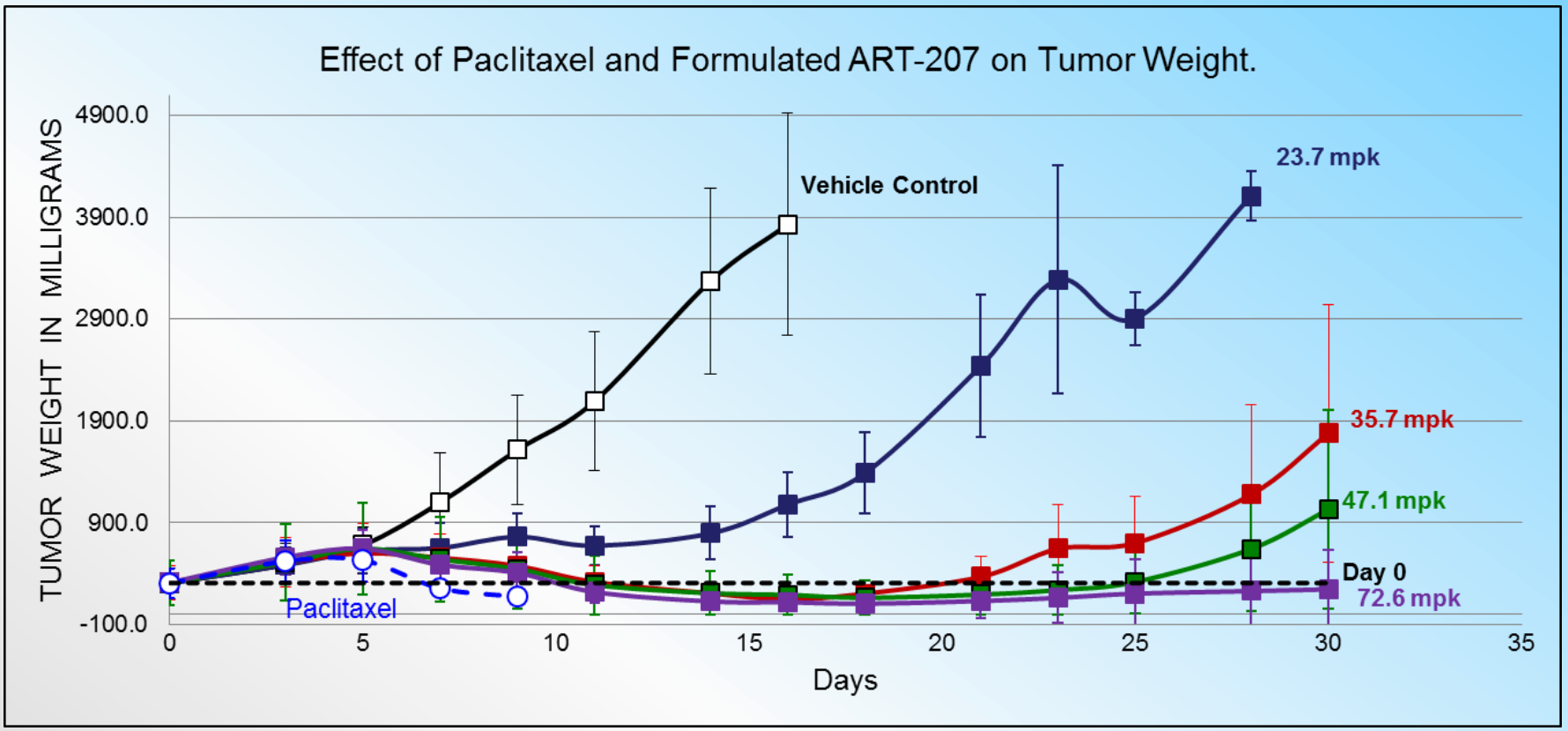
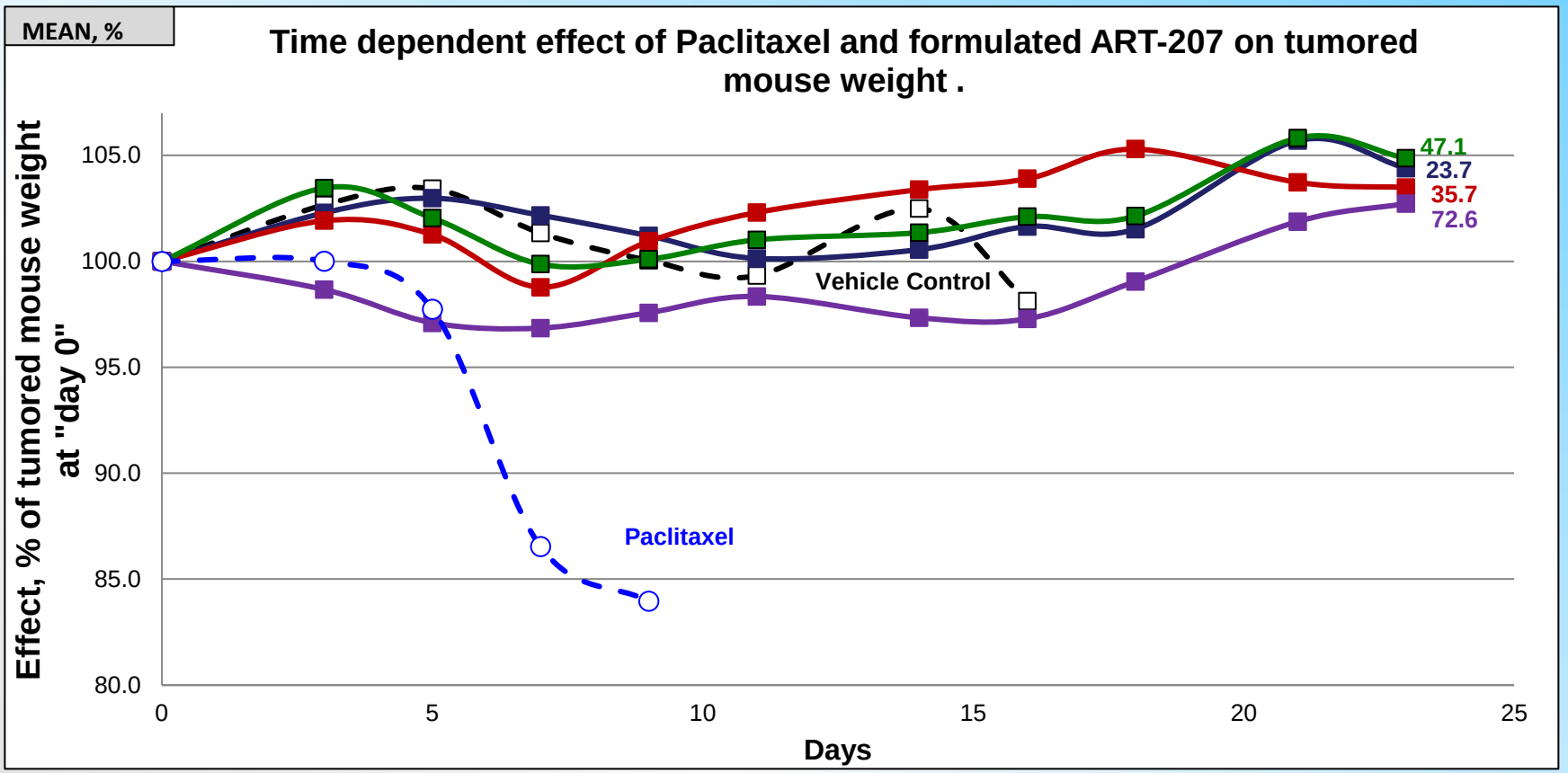
In Vivo Q1Dx5 MTD Nude Mouse



Mice were divided into 6 groups (5 mice in each group). All test articles were administered to mice for the five consecutive days via intravenous (iv) injections. Group #1 received drug-free lipid formulation ([0], open squares) and groups 2-5 received 23.7, 35.7, 47.1, and 72.6 mg/kg of formulated ART-207 (filled squares). Group #6 received 15 mg/kg of Cremophor EL/EtOH paclitaxel (open circles). Each point on the curves represents mean mouse weight assessed for each drug and vehicle treated group at the day of assessment (indicated in graph). The mean group cutoff is two animals per group. Effect is expressed as % of mean mouse weight assessed for each group prior to the first treatment at Day 0.

TumorSelect® Paclitaxel vs Taxol® Mouse Weight



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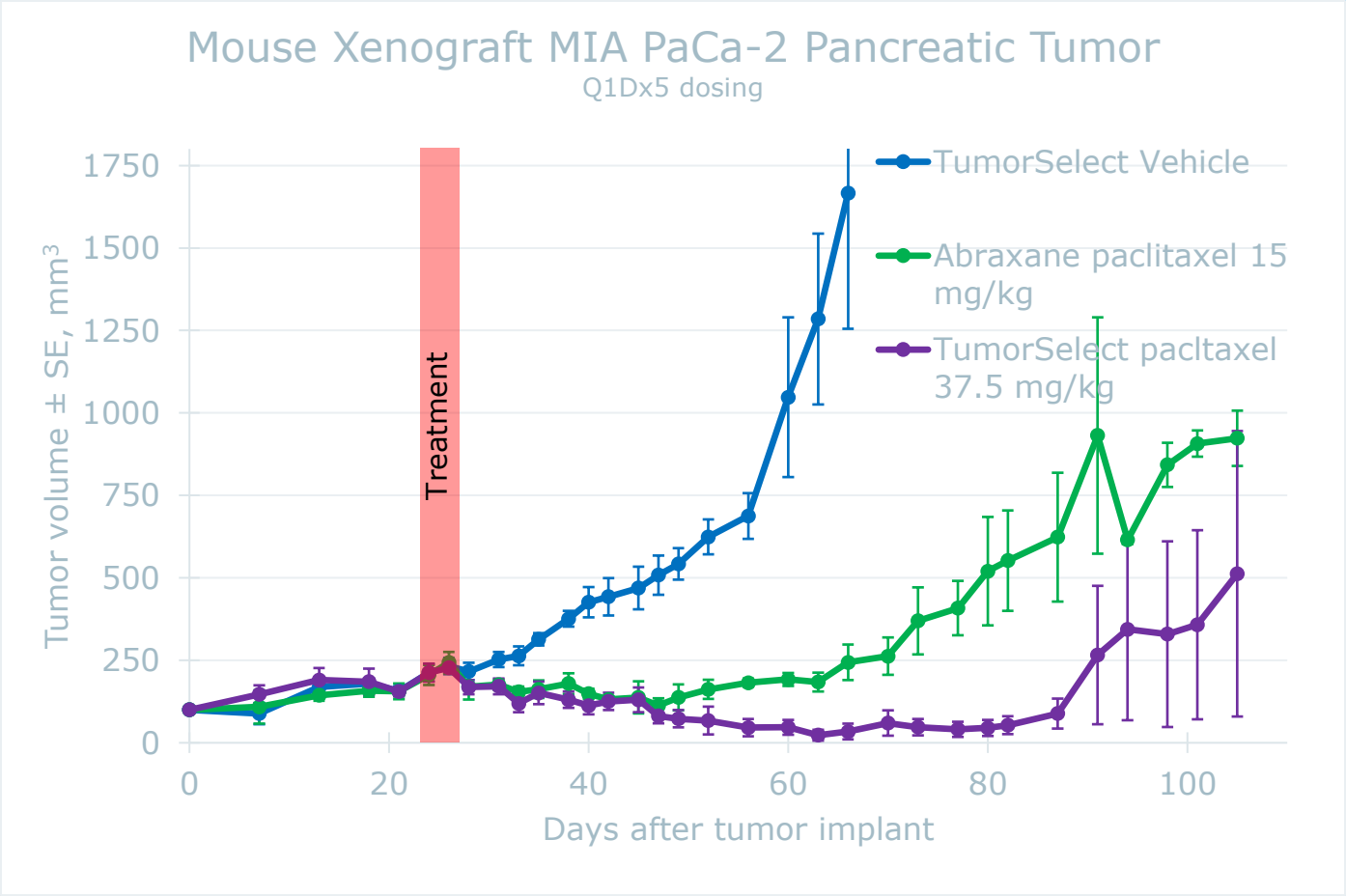
Pancreatic Growth Comparison to Abraxane®



MIA-PaCa-2 (ATCC, Manassas, VA) was implanted in NOD scid (NSG) female mice, and the animals were dosed with TumorSelect® paclitaxel with a comparison positive control of Abraxane®

Do We obtain Tumor Selective Delivery?

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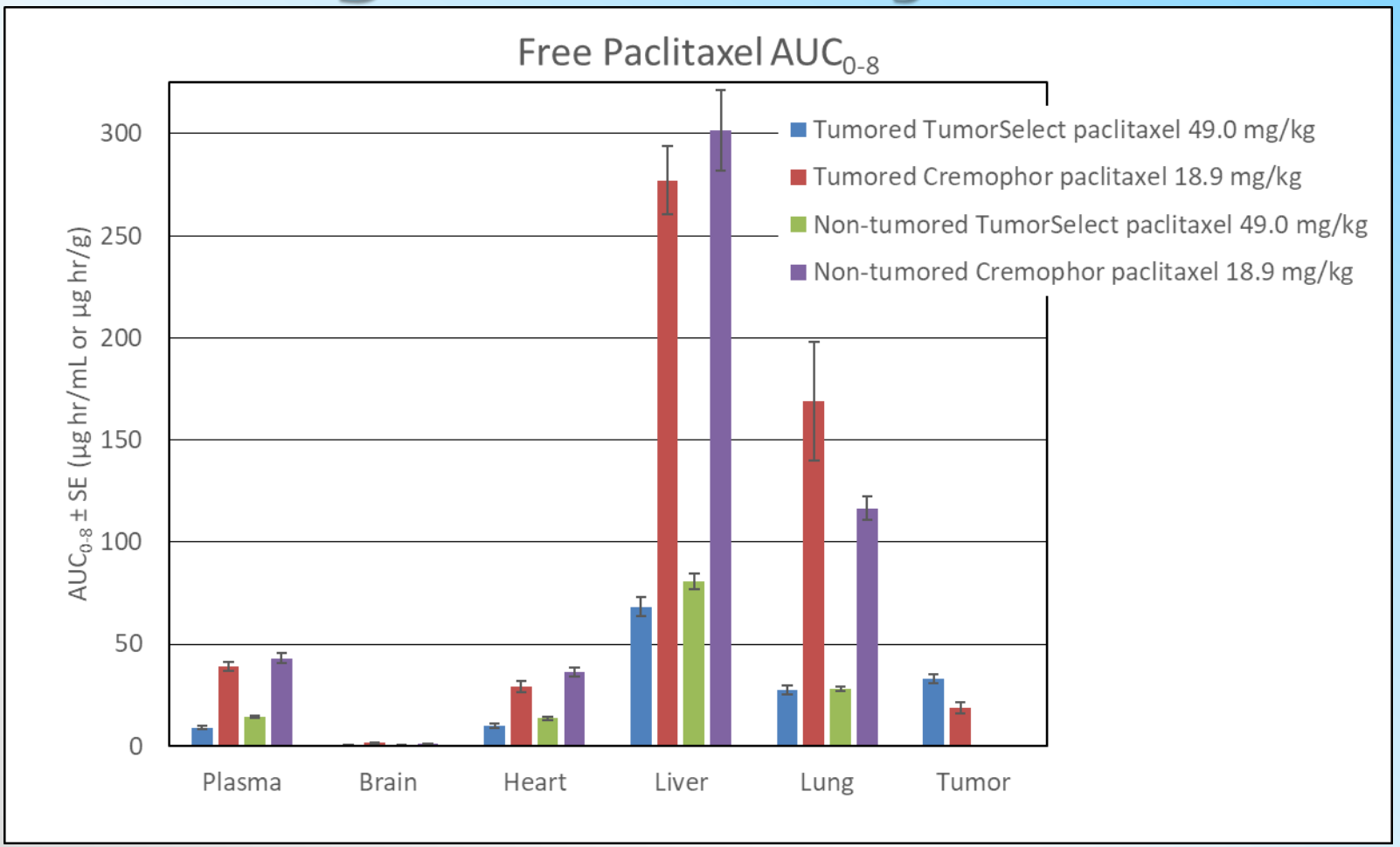
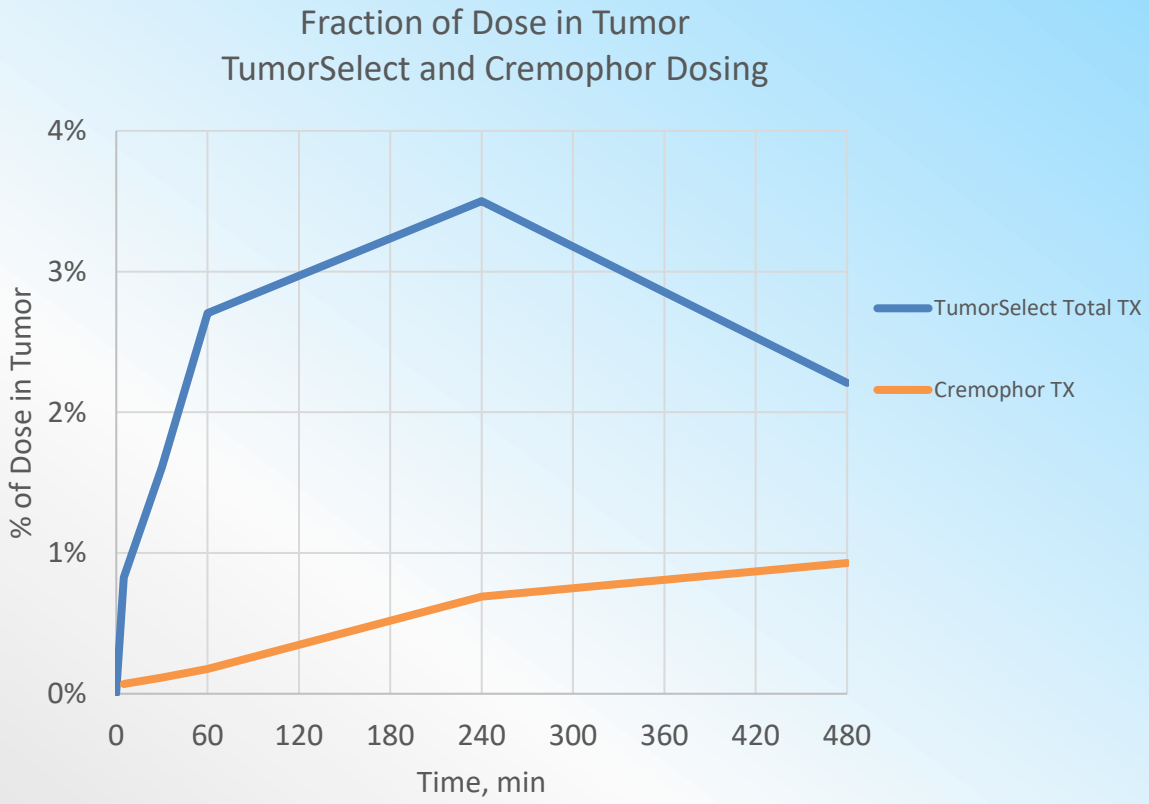
TumorSelect® Paclitaxel vs Cremophor®/EtOH Paclitaxel Single Bolus Injection



Delivery Efficiency of TumorSelect® Paclitaxel



Over 480 minutes, the delivery efficiency of total TumorSelect® paclitaxel is 4.8-fold higher than that of Cremophor®/EtOH paclitaxel

TumorSelect® Paclitaxel vs Taxol® Volume of Distribution

- **Non-tumored Animals:**
  - **TumorSelect® paclitaxel** **88 mL/kg**
  - **Taxol® paclitaxel** **658 mL/kg**
- **Tumored Animals:**
  - **TumorSelect® paclitaxel** **97 mL/kg**
  - **Taxol® paclitaxel** **567 mL/kg**

N.B. TumorSelect® paclitaxel remains in the vasculature and does not indiscriminately distribute the toxic chemotherapeutic to normal tissues and organs as does Taxol®

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TumorSelect® Paclitaxel vs. Taxol®

- **Overall TumorSelect® paclitaxel toxicity, efficacy and PK data show:**
  - **Tumor growth suppression**
  - **Less toxicity allows higher dose intensity**
  - **Slower tumor regrowth / increased duration of efficacy**
  - **Increased survival**
  - **Higher number of tumor-free animals**
  - **Significantly lower concentrations of paclitaxel in non-target tissues**
  - **Significantly higher concentrations of paclitaxel in tumor tissue**
  - **The time-averaged delivery (intact prodrug plus free paclitaxel) is 3.27% of the prodrug dose at 480 minutes**

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TumorSelect® Paclitaxel vs. Taxol® Summary

Data demonstrate targeted drug delivery and support LDL-receptor dependent mechanism of selective cellular uptake by tumor tissue of TumorSelect® formulated paclitaxel

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The Future of Clinical Practice

- **Clinical practice for the foreseeable future will continue to rely on cytotoxic chemotherapy with hundreds of thousands of patients treated annually.**
- **It is clear from published studies, such as the NEJM atezolizumab plus Abraxane® in triple-negative breast cancer study, that traditional chemotherapy will remain a mainstay of cancer treatment for the foreseeable future.**
- **In particular, there is evidence that taxanes can potentiate immunotherapy.**

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Conclusion
Enhanced Patient Benefit

- **TumorSelect® technology represents a major improvement in the clinical treatment of cancer through enhanced efficacy due to tumor-facilitated targeted delivery and reduced patient toxicity with its associated deleterious side effects**
- **Reduction of side-effect toxicity of cancer therapy by our technology will improve patient quality of life, patient retention in treatment regimes, more rapid patient recovery post treatment, and overall patient benefit.**

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Contact Information

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Thank you for your attention.

Questions????

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