Califia Pharma

San Diego, CA

Targeting Drug Resistant Cancers

Presentation

May 4, 2023

The Challenge

Solid-tumor cancers are the highest area of unmet need representing 90% of all adult cancers

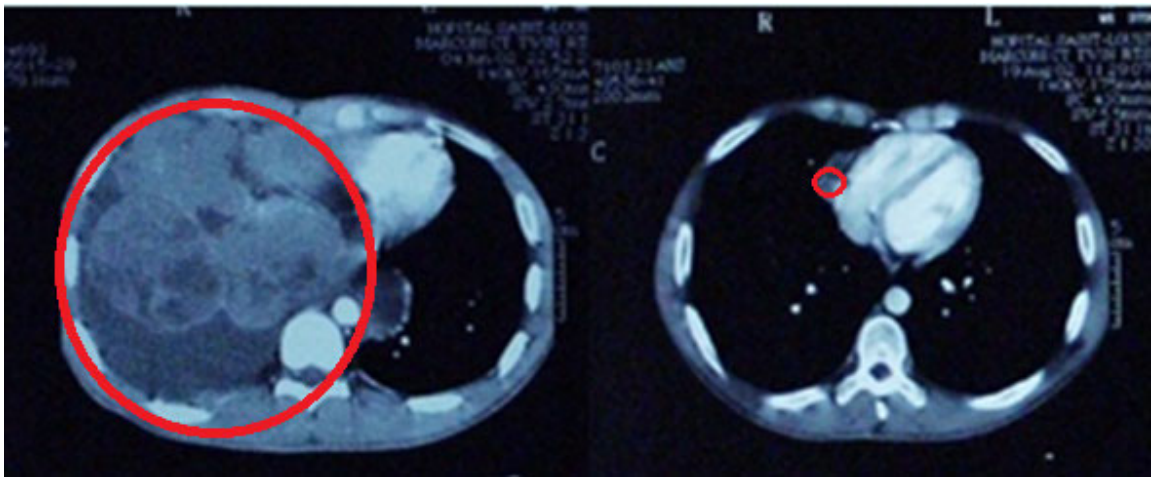
Current treatments are ineffective against our lead targets: drug resistant Ovarian, Liver, Sarcoma, and Prostate cancers

Califia's drug, CAP-0121, is a solution

- CAP-0121 has been 35 years in the making
  - Illudins are toxic chemicals derived from mushrooms
  - They are too toxic to be used in their natural form (but have been modified by Califia's founder)

- Human trials for 1st gen drug (irofulven, invented by Califia's founder) in 1200 patients demonstrated:
  - Strong responses (e.g., ~20% response in ovarian cancer)
  - Relatively low toxicity (except thrombocytopenia, low platelet counts). NO stomatitis, hand foot syndrome, peripheral neuropathy, liver damage, or renal damage common with other cancer drugs

Human irofulven trials showed some striking results



- 18-year-old sarcoma patient who failed multiple chemotherapeutic regimens and radiation therapy. Tumor outlined in red.
- Left: tumor compressed heart and lungs. Hard to walk or breathe
- Right: marked reduction in tumor size after three rounds of irofulven. No surgery involved during therapy.

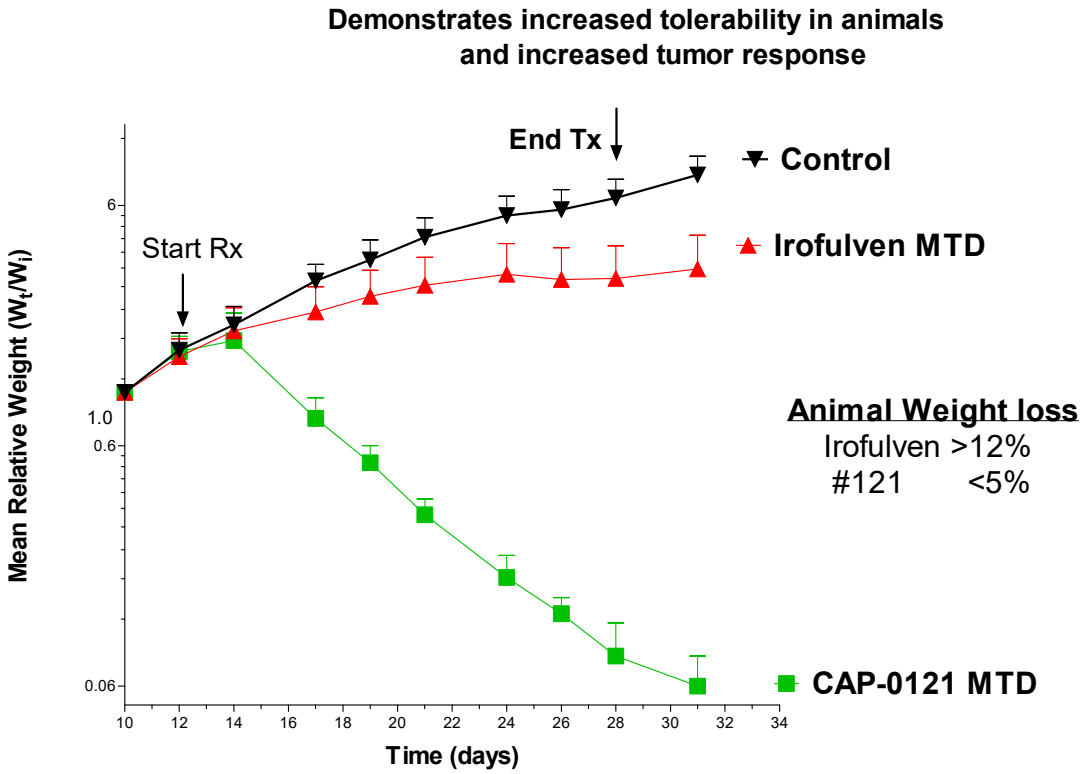
Additional images for ovarian, liver, and prostate cancer available in the data room

Why CAP-0121? What is different now?

- CAP-0121 is a better drug than irofulven
  - We screened 400 analogs of irofulven. Of these, CAP-0121 shows the best efficacy and lowest toxicity
- We now understand which patients will respond best
  - Illudins work by damaging DNA (a unique damage, compared to other drugs)
  - This damage is normally repaired by the TCR DNA-repair pathway
  - About 20% of cancers downregulate TCR repair ("TCR negative" cancers)
    - These cancers can't repair damage by illudins
    - These cancers are thus 30 to 100x more sensitive to illudins like CAP-0121
    - We believe this is why only 20% of irofulven patients showed a response
- We will use a companion diagnostic to screen for (and only treat) TCR-negative cancers
  - Such precision medicine screening was not possible with the prior drug (irofulven)

CAP-0121 has superior efficacy in mice

- Califia implanted a human-derived **drug-resistant metastatic** MV522 lung adenocarcinoma xenograft into mice.
- This model is resistant to over 35 anticancer drugs.
- Tumors in the control mice grew 6x in 30 days.
- Tumors in the irofulven-treated mice grew less quickly, but still grew 3x in 30 days.
- Tumors in the CAP-0121 (20mg/kg) group were eliminated by the end of 30 days, when therapy ended, and there was no recurrence of tumor in the next 30 days (**complete regression**).



Initial indications will be ovarian and liver cancer

- Currently no branded therapies, no cure for taxane & platinum-resistant cancers
- Available patient population of responders is ~40%
- Ovarian Cancer
  - 5-year survival rate for late-stage ovarian cancer is just 17%

    90% of all ovarian-cancer patients are diagnosed late stage
  - 188,867 women in US living with ovarian cancer: $1.2b market 2022
- Liver Cancer
  - 5-year survival rate is 20% with late detection
  - 235,650 people in the US living with liver cancer. $1.48b market by 2026

Limited Competition: Illudofulvenes only known drug class to block the TCR pathway

- Ovarian
  - Astra Zeneca, Tesaro, Roche, Pfizer, Novartis for maintenance therapies
- Liver
  - Q BioMed, ABVC Biopharma, Trillium Therapeutics, CASI Pharma, Sesen Bio for maintenance therapies
- Cell and gene therapies on the horizon, but no approved therapies or advanced trials

DNA Repair Pathways - Clinical Success

- Cancers, by their very nature damage cell machinery, including DNA repair pathways
- In addition to the Nucleotide Excision Repair pathway, which includes the Global Genomic Repair and the Transcription Coupled Repair (TCR) pathways, there are seven other known repair pathways including the Mismatch Repair Pathway
- The Mismatch Repair Pathway has been targeted with Jemperli (dostarlimab-gxly)
  - In a drug trial tumors vanished in all 14 patients diagnosed with early stage rectal cancer. https://www.washingtonpost.com/health/2022/06/08/cancer-drug-trial/
  - All patients shared the same genetic signature
  - FDA approved August 2021
- dostarlimab-gxly was developed by Tesaro, which GSK paid $5.1B for in 2019.

Results with MMR deficient cancers validate our approach for TCR deficient cancers

Non-over lapping patient population (MMR & TCR deficient are separate populations)

TCR population 4 times larger, and no competitors (numerous competitors exist for Jemperli)

Three Independent External Validations of Our Approach

Memorial Sloan Kettering (Tokpa, et al.)
https://pubmed.ncbi.nlm.nih.gov/33199492/

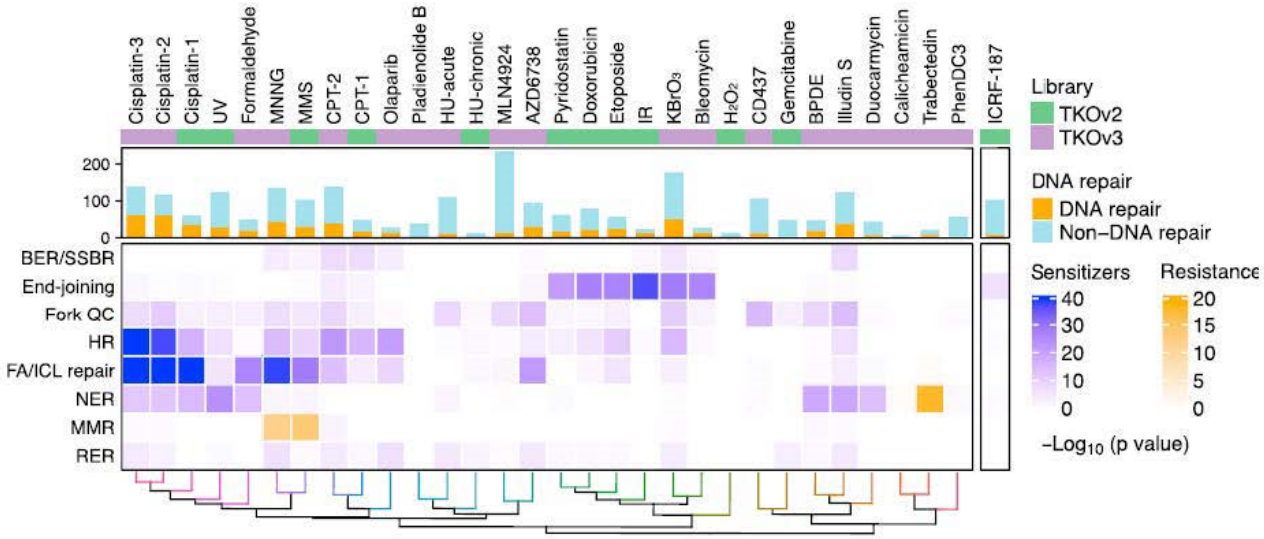
Dana Farber (Börcsök, et al.)
https://pubmed.ncbi.nlm.nih.gov/33208343/

European Consortium (Prosz, et al.)
https://www.biorxiv.org/content/10.1101/2023.02.07.527498v1

- Confirmation of the incidence of TCR-deficient cancers (ERCC2 or ERCC3) in breast, bladder and renal cancer.
- Confirmation that these TCR-deficient cancers express high levels of PTGR1 and are extremely sensitive to Illudofulvenes (including xenograft studies).
- Confirmation that pharmacologically achievable first generation drug levels achieved in humans are sufficient for killing TCR-deficient human cancers (based on 1 hour AUC).

Editorial on the importance of these studies to treating cancer
https://pubmed.ncbi.nlm.nih.gov/33472911

CRISPR Studies also validate our approach



CRISPR studies confirm the role of PTGR1 in conferring sensitivity to illudofulvenes as well as identifying that a deficiency in components of the TCR pathway resulted in a high sensitivity of tumor cancer cells to illudofulvenes. These 14 components included in our Companion Diagnostic are: ERCC1, ERCC2, ERCC3/XPD, ERCC4/XPF, ERCC5/XPG, ERCC6/CSB, ERCC8/CSA, GTF2H4, GTF2H5, RAD18, USP7, UVSSA, XPA. These studies also indicate that cancers deficient in base excision, fork and homologous repair would also be sensitive to illudofulvenes.

Califia has a strong patent estate

- 8 US patents granted (2016 – 2023) that cover:
  - composition of matter (hundreds of analogs)
  - use with companion diagnostic
  - use in Antibody-Drug Conjugates (ADCs)
- 4 US patent applications published and pending
  - Additional patent applications not yet published
- European and Canadian versions of the above US patents

Beside CAP-0121, Califia has another strong product

- CAP-0121 is an illudofulvene designed for administration as monotherapy
  - it has 4X the potency of the first generation drug (irofulven)
  - it is now targeted at specific sub-populations (genetically defined cancers)
- Califia has developed different illudofulvenes
  - far too toxic for direct administration as a drug, but great for use an ADC payload
  - displays a higher efficacy/toxicity ratio than MMA, the leading ADC payload
  - do not require PTGR1 activation or that the tumor be TCR deficient
  - Califia has also developed unique antibody linkers

Together, the payloads and linkers should be attractive to companies developing ADCs*

*Astellas paid $90 million to Sutro for access to its proprietary ADC platform (June, 2022)

Beyond CAP-0121, ADC Technology

Compare Cytotoxicity observed by the NCI

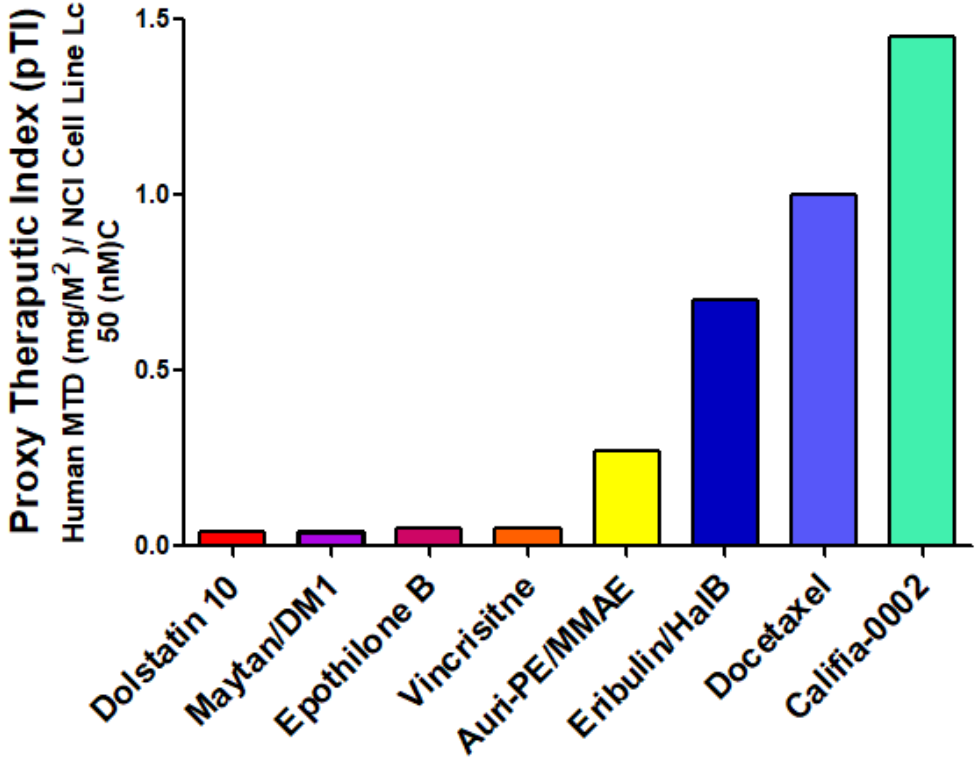
Mean Toxicity Data from NCI DTP 60 cell line			
Drug/NSC#	**Mean GI50 inhibition**	**TGI50 cytostasis**	**Mean LD50 cytotoxic**
Pyrrolobenzodiazepines 709119 monomer	10 nM	65 nM	> 10,000 nM
Pyrrolobenzodiazepines 694501 dimer	7 nM	302 nM	> 23,000 nM
DM1 791789	7 nM	11,700 nM	> 45,000 nM
MMAE 791792	8 nM	11,000 nM	> 50,000 nM
Duocarmycin SA 791790	1 nM	48 nM	> 8,500 nM
Tubulysin A (from Kuar, 2006)	12 nM	1,318 nM	> 10,000 nM
Halichondrin B 609395	2 nM	200 nM	> 1,000 nM
SN38 107124	35 nM	835 nM	> 10,000 nM
Epithilone A 791791	17 nM	85 nM	> 100,00 nM
Califia TCRI Payload “A”	10 nM	64 nM	511 nM
Califia TCRI Payload “B”	3 nM	20 nM	390 nM

*

Califia’s TCR Inhibitors are true cytotoxics at nanomolar level, yet they are 100 fold less toxic to animals (LD50, mg/kg)

Beyond CAP-0121, ADC Technology

Novel linker binding sties (to link payload to antibody)
Illudin payloads superior than current payloads in NCI DTP assay



We plan to out-license ADC tech to pharma.

This would reduce cash required to develop CAP-0121

Beyond CAP-0121, ADC Technology

Compare TCRI MDR Activity versus other payloads

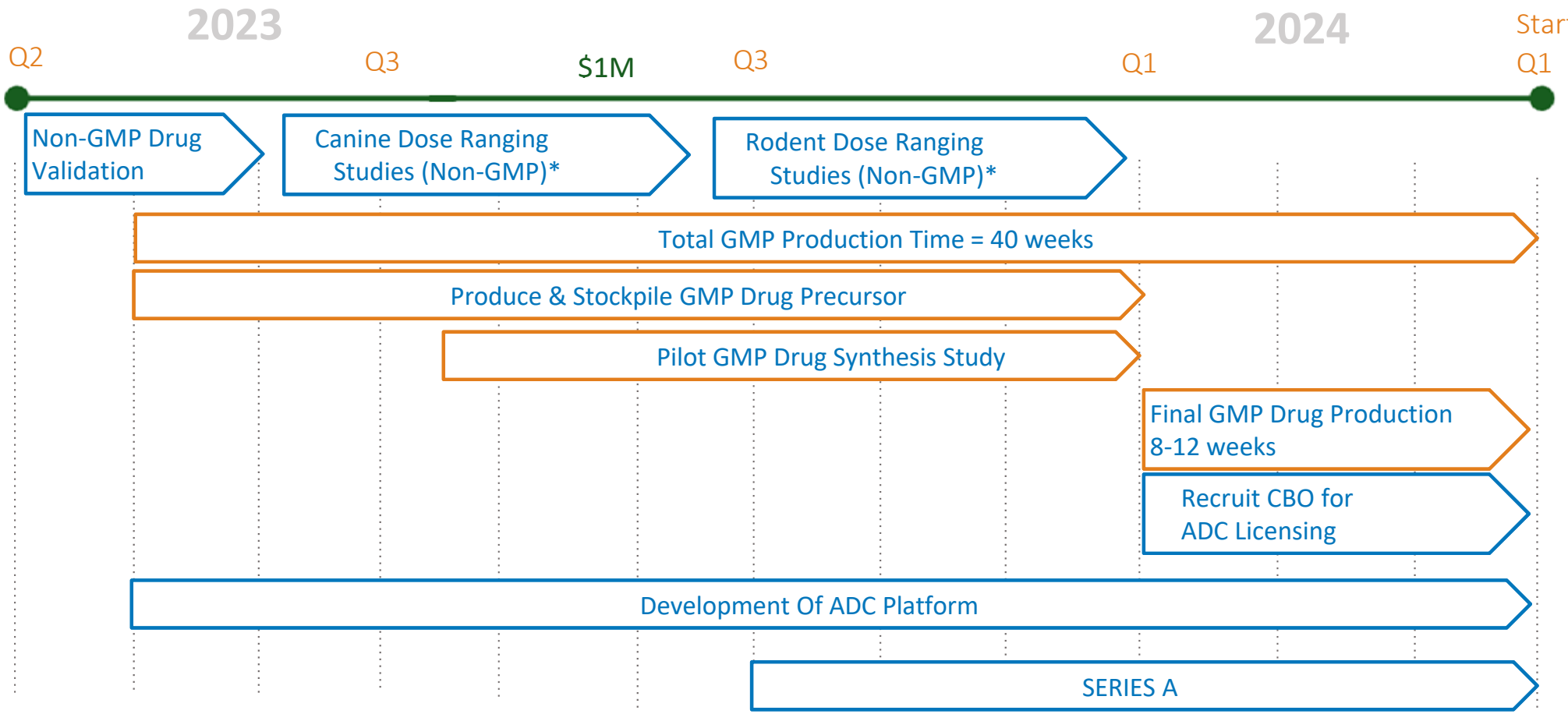
Payload	Resistance By MDR1	Resistance By MRP1	Resistance By BRCP
Califia TCRI Payloads	No	No	No
Calicheamicins	Yes	Yes	?
Anthracyclines	Yes	Yes	Yes
SN38	Yes	Yes	Yes
Taxanes	Yes	Partial*	Yes
Maytanasoids	Yes	No	?
Dolastatin/Aurisatins	Yes	Yes	?
Vinca compounds	Yes	Yes	?
CC1065	Yes	Yes	?

*MRP3 confers resistance to maytansanoids

Use of Funds for the next year

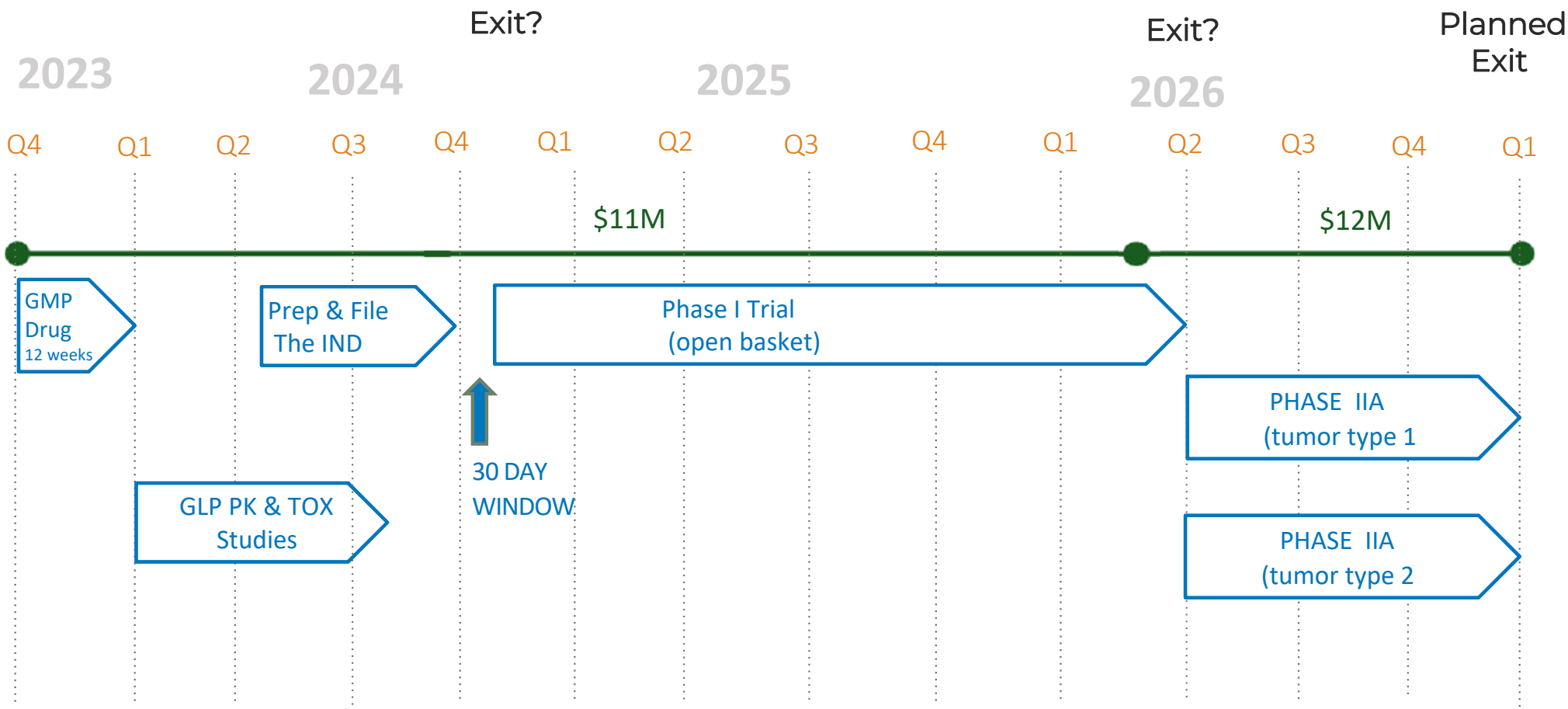
- Complete canine and rodent dose-ranging toxicity studies
  - VCs want these before funding our GLP tox and phase I clinical trials
- Complete ADC payload+linker combinations
  - Ready-to-ship material will expedite evaluations and deals with partners
- Complete the slower first part of drug production
  - Fungi grow slow. This stockpile will speed drug production after Series A
- Pilot scale GMP synthesis of CAP-0121
- Recruit a CBO to partner our ADC toolkits (to start upon Series A)
- Complete pre-IND meetings with the FDA (both CMC and Pharm/Tox)
- (No salary for CEO until Series A)

Time line for the next year



* Dose ranging studies include preliminary Pharmacology/Toxicology studies

Path to exit (after completion of Series A)



Phase IND/Phase I $11 million; Phase 2; $12 million. We anticipate that some of the required funds will be generated by (non-dilutive) licenses to our ADC tools

Exit Strategy: Current plan is to exit after phase 2a in 4 years

Exit	Possibility	Value
After IND	Possible* (but not desirable)	35M?
After Phase 1	Possible	350M-700M?
After Phase 2	Strategy	1.5B - 2.0B**

*Discussions with large pharma indicate early exit possible but not desirable
**Comparators for phase 1 or a phase 2 exit – next slide

Califia Leadership Team: Experience developing 1st Gen

Michael Kelner, M.D. M.S.
Founder, CEO

Dr. Kelner is a tenured Professor at the UCSD School of Medicine, and the co-discover and developer of Illudofulvens including Irofulven and CAP-0121. He has 35 years of oncology drug development and served as Chief Scientific Officer (CSO)/Chief Medical Officer (CMO) for pharmaceutical companies, as a consultant to companies during acquisition of anticancer agents, and overseen implementation of oncology phase III trials. He was the principal investigator on research grants totally more than $10 million and served on numerous NIH review committees.

Chief Business Officer
TBD

Current plan is to hire a seasoned CBO with expertise in ADCs to out-license Califia's other assets.

Anthony Craig, J.D., Ph.D
Co-Founder IP Attorney

Anthony Craig has been practicing as an Intellectual Property attorney for over20 years and has extensive experience in protecting chemical, biological and pharmaceutical inventions . He has previously worked in various capacities for a number of start-up biotech ventures, Bio-Ion Nordic AB (ABI Biosystems), SciMarket Strategies Inc. and Cognetix Inc.

Steve Weitman, M.D., Ph.D.

Director of the Institute for Drug Development at the CTRC, University of Texas, San Antonio

Dr. Weitman is former Interim Chief Medical Officer for Immunogen leading their ADC development program and has also served as Chief Medical Officer and Senior Vice President at ILEX Oncology. His goal is to create and support oncology drug development, build experimental phase I and phase II programs and develop individualized patient cancer treatments involving both laboratory and clinical teams. He was involved with development of the 1st gen drug and personally administered it to his patients.

The management team also includes the remainder of the 1st generation team: CMC/manufacturing, Pharm/Tox and Clinical Team

Exit comps suggest potential for $1.5b to $2.0b exit within 3 years

Direct Acquisition by Major Pharma after phase 2 trials See Forbes 4/22/2015: Are M&A replacing R&D for Pharma?		
Company	Acquired by	Acquisition Value
AliosBio (2015) Phase 2	J&J	$ 1.7B
Ogeda (2017) Phase 2a	Astellas	$ 1.1B
IFM Ther (2019) Phase 2a	Novartis	$ 1.6B
Agios (2020) Phase 2	Servier	$ 1.8B
Kymab (2021) Phase 2	Sanofi	$ 1.4B
5 Prime Therapeutics (2021) Phase 2	Amgen	$ 1.9B
Turning Point, repotrectinib (2022)	BMS	$ 4.1B
Affibody (2019) Phase 1 (only)	J&J	$ 0.7B

Patient populations for the above acquisitions were less than 50,000 annually, versus 500,000 for Califia Pharma's lead drug

Risks & Mitigation

We are an early stage biotech company facing the usual hurdles:

- **Securing an IND**
- **Raising enough money to conduct clinical trials**
- **Demonstrating success (efficacy plus a lack of major systemic toxicity) in those trials**

Toxicity: There is always a risk when translating to humans, but there is a lower risk due to our experience with 1200 human patients (first gen drug). Our new compound, CAP-0121, was specifically designed engineered to be less toxic than the prior drug (decreased toxicity but superior efficacy is now confirmed both *in vitro* and *in vivo*).

Efficacy: There is always a risk translating to humans. Risk is now reduced as we understand the mechanism of action in detail. Unlike the prior drug, we now understand how this class of drugs works, and most importantly, specifically what molecular signature(s) are required in the cancer to allow the drug to function. Our companion diagnostic will allow selection of these patients, which should produce very strong efficacy "readouts" or clinical responses.

Financing: There is a risk that we get through the IND process but can't secure funding for a phase 1. We believe that the size of our target market, the superior efficacy and safety profile, and strong IP/patent protection will well position us to raise a series A to begin trials. If we have success licensing our ADC toolkit to ADC focused companies (over 120 exist), our need for external funds will be reduced.

Execution: I have directly managed 3 drugs through clinical trials (phase I, phase 2, phase 3) and functioned as a CSO or CMO. I have not run a company as CEO but handled annual budgets in excess of $10 million. With these funds I plan on hiring a director of BD to license our ADC toolkit. As we progress close to IND and Series A, I plan on hiring a new CEO with proven experience successfully running early stage biotech/biopharma startups.

Next Step a CDA → Data Room

- Science behind CAP-0121
- In vitro cytotoxicity studies
- Multidrug-Resistant (MDR) studies
- Xenograft/Animal studies
- Toxicity Studies (e.g. platelet count)
- Synergy Studies (other cancer drugs)
- Unique mechanism of action data
- External validation: MSKCC, Dana Farber, European consortium (Prosz) (incidence of TCR deficient cancers, PTGR1 expression, Drug sensitivity and PK relationship)

- Supporting Evidence
- Patents & patent applications
- Publications & presentations (Califia & others)
- IND Planning (RFPs, Returned bids, and budget)
- Phase 1 and Phase 2a Clinical Trials
- Companion Diagnostic Technology
- ADC/SMDC platform studies

Upon execution of a CDA, a data room is available containing all relevant scientific data of the drug, as well as the business aspects of Califia Pharma, Inc.

Califia Pharma

Summary

- Multiple patented technologies
  - CAP-0121, a powerful, safe precision medicine with companion dx for multiple types of solid tumors
  - ADC payloads and linkers
- Experienced management team will
  - Drive CAP-0121 through clinic
  - Out license ADC technology

Additional details and SeedFolio's review available at:

https://app.box.com/s/esq4x6g26rwaf9gsqky2lr7dua00aa78

Thank you

Michael Kelner
Chief Executive Officer
Califia Pharma, Inc.

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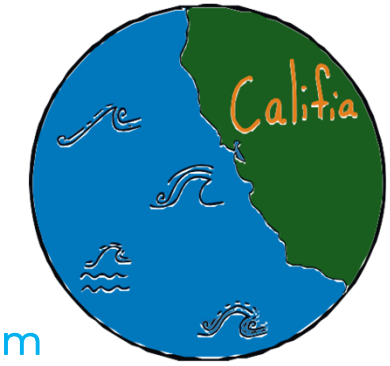

PARTNERS

UCSD

UPPSALA UNIVERSITET

Karolinska Institutet

NIH NATIONAL CANCER INSTITUTE
DCTD Division of Cancer Treatment & Diagnosis

PRECISION seedfolio ULU VENTURES

Califia Summary

- 35 years of R&D. New company. New patents *granted* with coverage until 2040
- Prior drug, tested in 1,200 patients, 20% response in cancers with only mild toxicity
- Next-gen drug CAP-121 is superior and safer
  - CAP-121 eliminated tumors in a drug-resistant metastatic mouse model
  - Now a pro-drug with 4x greater therapeutic index
- MOA is now understood. Works in the 20% of cancers that are TCR deficient
  - We will utilize a companion diagnostic to treat only likely responders
- Raising $1.2m to complete pre-clinical through IND (600K committed to date)
- Priced round with $10m pre. Exit potential of $2b+
- Management team seasoned with oncology experience
- Califia's ADC platform may provide an additional source of non-dilutive funding.