

# TildenBio Customer Outreach Deck

## 1. There is a problem.

Mammalian cell tissue culture is critical to biomedical research and to the production of many blockbuster drugs, as well as future gene therapy vectors. Animal-sourced sera provide the growth factors and cytokines that are essential for tissue culture. Bovine sources such as fetal calves represent a major share of the market.

There are a number of problems with this.

a) The supply is finite and inadequate, driving up price.

Tissue culture production costs determine if effective anti-cancer drugs can profitably enter the market.

The size of the market of those that do enter is limited by willingness-to-pay by the health insurance industry.

The cost of sera has been, and is increasingly detrimental to grant-dependent research.

The current cost of sera makes expansion to larger markets such as the cultured meat industry unrealistic.

b) Animal-sourced sera is inherently problematic as a product.

i) It is variable and ill-defined, which is detrimental in an industry that depends on limiting variables.

ii) Animal-sourced sera can contain contaminants such as endotoxins and can harbor human pathogens like viruses, bacteria, fungi, mycoplasma, and prions that cause mad cow/Creutzfeldt-Jakob disease. Certifying sera pathogen-free adds greatly to the cost of research and to the cost of any production that requires sera.

## **2. It is a big problem.**

There is growing political opposition to animal-sourced biomedical proteins.

Large markets such as the EU increasingly recognize that current sources of biomedical proteins incur animal suffering. For example, the Joint Research Centre of the European Commission's Science and Knowledge Service/EU Reference Laboratory for Alternatives to Animal Testing recommends that animals should no longer be used for the development and production of antibodies for research, regulatory, diagnostic and therapeutic applications. Further, they recommend that "EU countries should no longer authorize the development and production of antibodies through animal immunization, where robust, legitimate scientific justification is lacking for animal use in a call for adherence to the legal obligations under Directive 2010/63/EU".

With respect to cytokines and growth factors from sera specifically, large markets such as the EU have animal welfare laws in place that prohibit the transport of animals in their later terms of pregnancy, which directly limits access to fetuses for sera (Regulation (EC) No 1/2005, 14 amending Directives 64/432/EEC and 93/119/EC and Regulation (EC) No 1255/97.15). Unfortunately, rather than reducing animal suffering, this has driven sera sourcing outside the EU. This outcome has led to discussions of an outright ban of animal-sourced cytokines and growth factors.

## **3. The problems with animal-sourced sera are recognized.**

The global tissue culture market is a tens of \$billions a year market, with consumables such as sera and the cytokines and growth factors representing the largest and fastest growing sector in that market. A number of big players such as Thermo Fisher Scientific Inc., Merck KGaA, GE Healthcare, Lonza, BD Biosciences, Sigma-Aldrich Corporation, Corning Incorporated, Irvine Scientific, STEMCELL Technologies Inc., PAN Biotech, MP Biomedicals LLC, PromoCell GmbH, AbCam to name but a few have a presence in the animal-free cytokine/growth factor market. Many niche companies exist in this

sector as well. The viability of the cultured meat market depends entirely on animal-free sera, with over sixty startups in this area. Significantly, larger players such as Merck have entered the cultured meat market.

However, attempts to overcome the problems associated with animal sera have introduced new problems. Current animal-free cytokines and growth factors are typically obtained from *E. Coli*, but bacterial expression introduces endotoxin and inclusion bodies, and can require expensive re-folding of proteins with poor recovery. These technical hurdles further increase the cost.

#### **4. We have a solution.**

TildenBio has a new, patented, photosynthetic protein production platform out of the Melis Lab at UC Berkeley. The synthetic biology platform makes biomedical proteins economically, simply and at large scale. Further, production is green and carbon-neutral, using sunlight and extracting CO<sub>2</sub> from the atmosphere.

#### **5. It's a great solution.**

We have achieved expression levels of over 20% of total cell protein. The system does not use antibiotics. Our bioreactors do not require rich media, heating or cooling, lowering the likelihood of batch failure. Further, our high yields lessen reliance on high percentage recovery, allowing lower cost purification methods. Our low-cost growth factors and cytokines can replace animal-sourced tissue culture sera.

#### **6. We are in discussion with potential partners.**

We are in early production discussions with multiple large pharmaceutical companies. Our business model is in response to their expressed desire to have partnerships in this area, and to meet their expressed needs.

**7. Our team can do this.**

Pioneering UC Berkeley Professor Tasios Melis

Jerry Riessen, CEO, serial entrepreneur

We are bringing in a biopharma CEO

Past and current Melis lab personnel are ready to join.

**8. The regulatory pathway is known and achievable.**

Cytokines and growth factors are commonly produced – they are expensive and they have contamination risks and harm animals.

**9. Our IP gives us a competitive advantage**

TildenBio has exclusive control of the UCB Melis Lab patents and UC Berkeley is an equity partner. The technology delivers low-costs, high-expression levels and high purity, allowing us to be competitive on price and quality.

**10. TildenBio will initially make cytokines and growth factors.**

With our own off-campus lab and more lab technicians, TildenBio would be set up for early profitability making cytokines and growth factors and would be well positioned to enter the diagnostics, edible vaccine and the growing cultured meat market as the business grows.