Pandemic Prevention Platform (P3)
Briefing to the Scientific Review Official
HR001117S0019

(b)(6)

(b)(6) DARPA/BTO

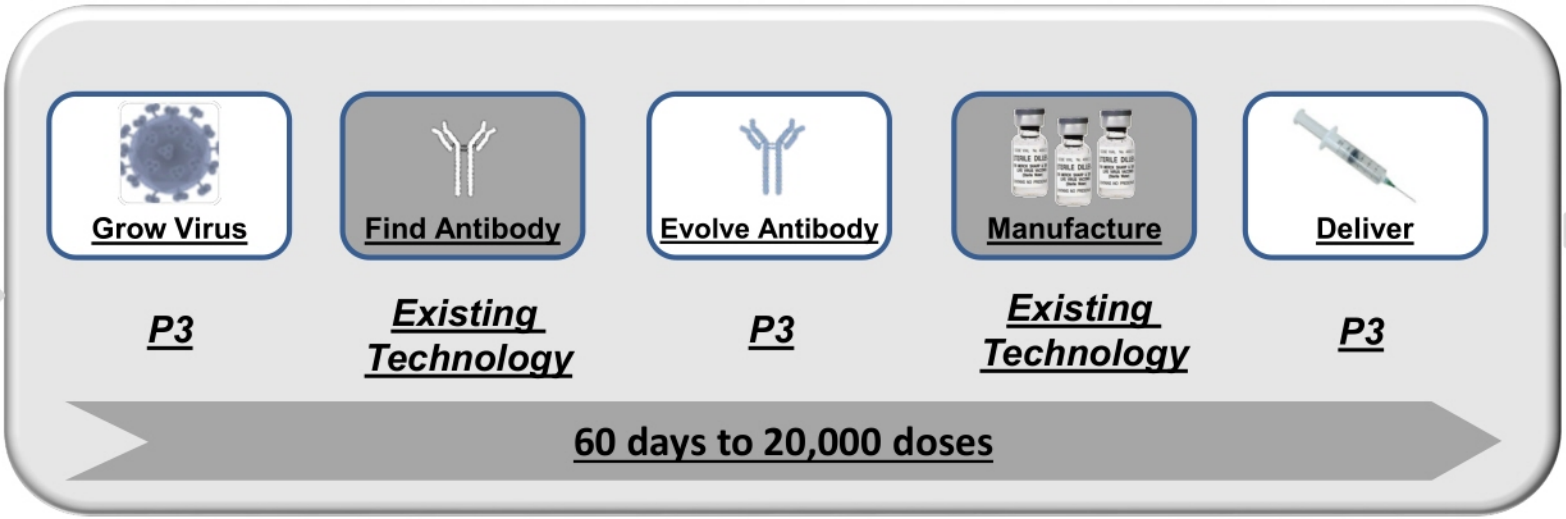
Briefing prepared for (b)(6)

June 27, 2017

Pandemic Prevention Platform (P3) vision

Develop a functionally integrated platform to deliver pandemic prevention treatments in <60 days

Pandemic Outbreak
Any Virus



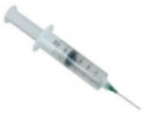
Treatment to Prevent Pandemic

State of the art pandemic response is limited

Current Challenges:

Grow Virus

Evolve Antibodies



Deliver Therapy

P3 will be an integrated platform to:

TA1: Grow unculturable and emerging viruses to test antibody therapy and quantify potency

TA2: Accelerate evolution of highly potent antibodies

TA3: Develop delivery methods for administration of gene-encoded antibodies to patients

P3 Program Metrics

Technical Area	Metrics
TA 1: On-demand platform to grow virus	• Amplify pathogen to a minimum 10^{13} infectious units (PFU or TCID50) within 72 hours post-inoculation • Pathogen genetic drift less than 0.1% after 5 successive culturing (growth) iterations (mutations per base pair per culturing cycle) • Progeny virus bio-identical to original isolate in lipid, protein, and carbohydrate content • Apply platform to five viruses representing at least one RNA virus, one DNA virus, and both (+)-sense and (-)-sense single stranded viral genomes
TA 2: System to evolve antibodies	• Ready for use in less than 72 hours • Demonstrate the ability to couple antibody discovery capability with the antibody evolution capability either through new discovery technologies or physical coupling with existing technologies • Support rapid potency maturation improving antibody/therapy greater than 100-fold in under 8 days • Apply technology to mature five different antibodies/therapies targeting at a minimum three (3) different pathogens representing at least one RNA virus, one DNA virus, and both (+)-sense and (-)-sense single stranded viral genomes
TA 3: Deliver medical countermeasure(s)	• Achieve greater than 10 µg/mL serum concentration of target medical countermeasure with peak production in <3 days post-injection in large animals • Minimally or low-invasive simple delivery method given at 1 delivery site • Demonstrate reproducible production (less than 10% variance in serum concentration) in large animals • Demonstrate 100% protection against performer defined pathogen challenge in animal models by day 3 post countermeasure administration • Demonstrate longevity of protection lasts for greater than 30 days
Platform Integration	All of the following metrics must be achieved within 60 days and must include full integration with the metrics for TA1-3: • Demonstrate the ability to identify a pathogen specific antibody/therapy for rapid affinity maturation in TA2 within 14 days • Demonstrate the ability to manufacture research grade genetic constructs for use in animal studies • Demonstrate the ability to manufacture clinical grade GMP material for human safety trials – this metric must be met for only one of the phase II demonstrations. The ability to scale-up manufacturing and distribution to 20,000 doses must also be addressed as part of this metric • Demonstrate safety and efficacy in animal models and in human clinical trials

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of the Freedom of Information Act.

BAA Specifics

- Was a projected funding amount and/or start date specified in the BAA?

  The BAA stated that "Multiple awards are anticipated" but no funding amount was identified.

  The FAQ indicated that proposals could anticipate start dates in Oct, Nov. or Dec. 2017.

- Is this basic (6.1) or applied (6.2) research? **6.2 (BT-01)**
- What, if any, GFE/GFI/GFP did the Government offer? **None**
- Is human or animal use anticipated/required? **Human and Animal Use is Required**
- Are there any unusual stipulations regarding intellectual property? **None**
- Does the program have multiple Technical Areas (TAs)? If so, please describe proposer requirements (multiple TA responses in a single proposal, must respond to all TAs, etc.)

  Yes - there are three technical areas and the BAA required that proposers address all three technical areas

- Other unique attributes of the solicitation here

  - The performers are required to propose and complete a Phase I clinical trial
  - The proposers are required to demonstrate they have the ability to integrate all three technical areas through capability demonstrations

Program Structure

Program Month:

0	3	6	9	12	15	18	21	24	27	30	33	36	39	42	45	48

Platform Development (30 months)

Integration/Capability Demo (24 months)

Capability Demonstration #1: Performer Pathogen Choice 3 months

Capability Demonstration #2: Performer Pathogen Choice 60 days

Capability Demonstration #3: DARPA Defined Pathogen 60 days

Fully Integrated Capability Demonstrations #4 and #5 (2x 60 day simulations)

Blinded pathogens

Base Period (24 Months) | **Option Tasks (24 months)**

Overall Structure

Performer Diversity to Maximize Platform Success/Use in the Future

RNA Platform

Vanderbilt University

Duke University

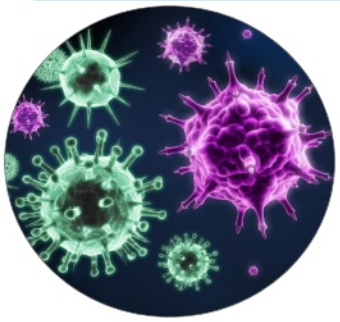
DNA Platform

AbCellera

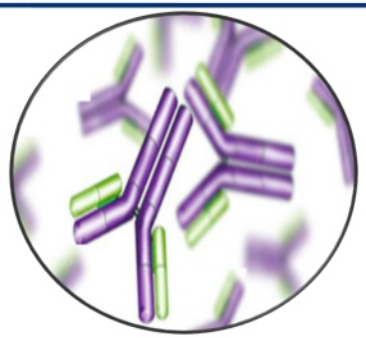
Head-to-Head Comparison Platform

MedImmune

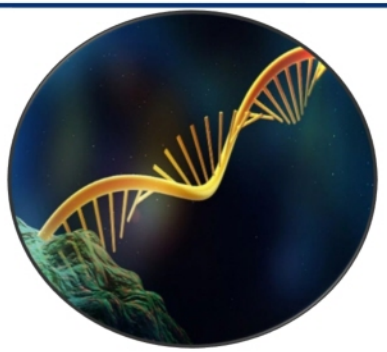
RNA Platform – Academic/NewCo Maintained



Grow viruses via traditional cell lines



Identify and mature antibodies from acute and convalescent patient samples



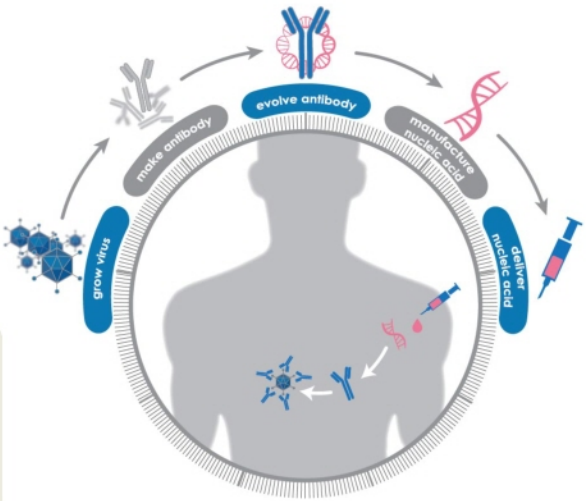
RNA-encoded antibodies for immediate protection from pandemic viruses

Vanderbilt

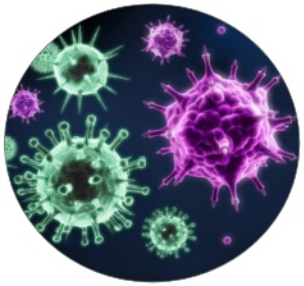
High-throughput screening → Human hybridoma & display technology → mRNA, replicating RNA & novel formulations for intramuscular (IM) delivery

Duke

High-throughput screening & synthetic virus from sequence → Mass spec sequencing of repertoire & computational evolution → mRNA & novel formulations for subcutaneous (SQ) delivery



DNA Platform – Biotech Company Maintained



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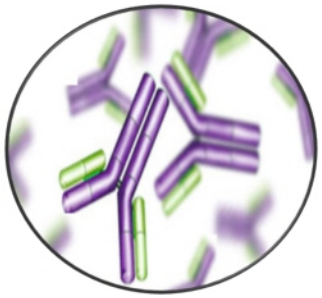
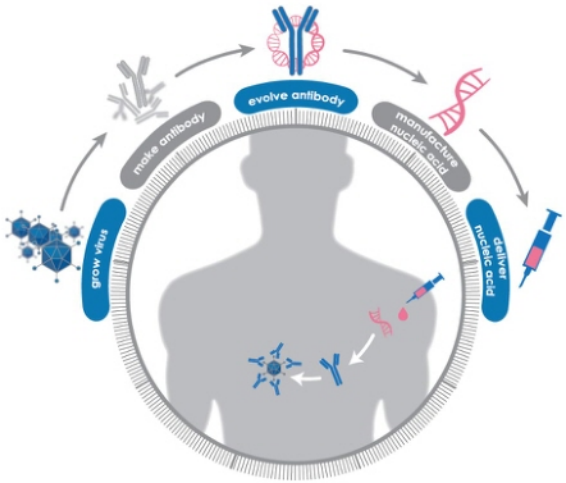


Identify and mature antibodies from acute and convalescent patient samples

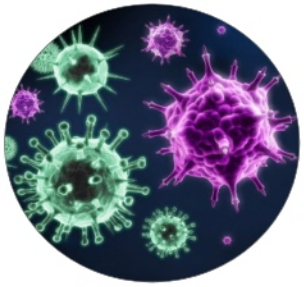
DNA-encoded antibodies for immediate protection from pandemic viruses

Abcellera

High-throughput screening → B-cell sequencing via microfluidic sorting & display technology → DNA delivery via electroporation of a cocktail of antibodies



Comparison Platform – Pharma Maintained



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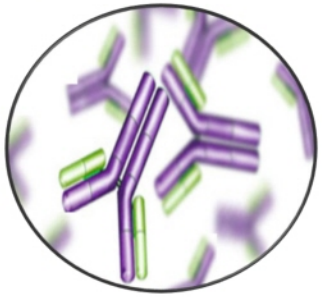

Identify and mature antibodies from acute and convalescent patient samples

DNA and RNA-encoded antibodies for immediate protection from pandemic viruses

Output of the built in downselect and program completion

MedImmune

Grow virus for commercially relevant targets

B-cell sorting and microfluidics technology

DNA delivery via electroporation

mRNA delivery via novel formulations

P3 Platform based on best technology tested head-to-head by Pharma

2 commercially viable targets (Influenza & RSV)

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