MEDI4893

- High affinity human anti- *S. aureus* alpha toxin IgG1 ($K_D = 89$ pM)
- Neutralizes all AT variants identified in >1,500 clinical isolates#
- Improves disease outcome in multiple disease models
- YTE mutations engineered into Fc region – improved 1/2–life
- Under development for the prevention of pneumonia in high-risk ICU patients

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#Tabor et. al., AAC, 2016; Sharma-Kuinkel et. al., JCM, 2015.

Oganesyan et. al., JBC, 2014
Benefits of antibodies as antibacterials

**Specificity**
- No perturbation of the beneficial microbiome or cross-resistance

**Safety**
- Potential to be safer due to pathogen specificity

**Long half-life**
- Single dose protection for up to 3 months

**Antibiotic preservation**
- mAb MOA will not select for resistance to small-molecule antibiotics

**MAb MOAs complementary to antibiotics**
- Enhance host bacterial clearance
MEDI4893* improves outcome in a murine pneumonia model

Improved Survival

Day elapsed

Percent survival

0 20 40 60 80 100

Log10(CFU/Organ)

USA300
3.1x10^8

mAb administered 24h prior to IN challenge

IN = Intranasal

Bacterial Load (CFU)

Lungs

Kidneys

P=0.011

P=0.06

Hua et. al, AAC, 2014.
MEDI4893* reduces disease severity in murine dermonecrosis model

Control IgG  MEDI4893*

Day 1

Day 7

Tkaczyk et. al, CVI, 2012.
MEDI4893 is being developed for prevention of ICU pneumonia in S. aureus colonized and intubated patients

◆ Current product has limited utility in L/MICs
  – Multiple grams dose pose economic barriers
  – Requires intravenous infusion
  – Requires pathogen specific (rapid) diagnosis

◆ Alternate development will be needed to broaden population
  – New technology being developed to express monoclonal antibodies in vivo with DNA, mRNA, viral vectors
  – Potency for soft tissue infection appears to be favorable and intramuscular administration in children may be feasible for mg/kg basis