Afrigen's RSV mRNA vaccine project

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Introduction - RSV

- Causes respiratory cold-like symptoms (spectrum of disease)
- Most common cause of hospitalization in infants
- Significant burden of disease in elderly (>65 yrs)
- Majority of deaths occur in LMICs & outside of hospital setting
- Mab treatment palivizumab/nursevimab (high income countries)
- No Licenced vaccine but Ph3 Pfizer/GSK/Moderna

- **34 million acute lower respiratory tract infections in young children**
- **3 million hospitalizations**
- **66000-199000 fatalities**
- **99% LMICs**

WHO, 2017

RSV infection and immunity

- Natural infection doesn't result in durable immunity and reinfection occurs throughout life
- Antibodies target viral envelope F & G proteins but F is well-conserved
- Nabs preferentially target prefusion F (PreF)
- RSV IgA and Nabs correlate with reduced infection risk
- Th1 response, IFN-y
- Th2 tracks with disease severity

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Russel et al., 2017

Stabilization of F protein in prefusion state

Pre-fusion F is absent on the surface of formalin-inactivated respiratory syncytial virus

April M. Killikelly, Masaru Kanekiyo & Barney S. Graham

Structure of RSV Fusion Glycoprotein Trimer Bound to a Prefusion-Specific Neutralizing Antibody

JASON S. MCLELLAN , MAN CHEN, SHERMAN LEUNG, KEVIN W. GRAEPEL, XIULIAN DU, YONGPING YANG, TONGQING ZHOU, ULRICH BAXA, ETSUKO YASUDA, TIM BEAUMONT, AZAD KUMAR, KAYVON MODJARRAD, ZIZHENG ZHENG, MIN ZHAO, NINGSHAO XIA, PETER D. KWONG , AND BARNEY S. GRAHAM fewer Authors Info & Affiliations

Structure-Based Design of a Fusion Glycoprotein Vaccine for Respiratory Syncytial Virus

JASON S. MCLELLAN, MAN CHEN, M. GORDON JOYCE, MALLIKA SASTRY, GUILLAUME B. E. STEWART-JONES, YONGPING YANG, BAOSHAN ZHANG, LEI CHEN, SANJAY SRIVATSAN, ANQI ZHENG, TONGQING ZHOU, KEVIN W. GRAEPEL, AZAD KUMAR, SYED MOIN, JEFFREY C. BOYINGTON, GWO-YU CHUANG, CINQUE SOTO, ULRICH BAXA, ARJEN Q. BAKKER, HERGEN SPITS, TIM BEAUMONT, ZIZHENG ZHENG, NINGSHAO XIA, SUNG-YOUL KO, JOHN-PAUL TODD, SRINIVAS RAO, BARNEY S. GRAHAM , AND PETER D. KWONG fewer Authors Info & Affiliations

Prefusion F–specific antibodies determine the magnitude of RSV neutralizing activity in human sera

JOAN O. NGWUTA, MAN CHEN, KAYVON MODJARRAD, M. GORDON JOYCE, MASARU KANEKIYO, AZAD KUMAR, HADI M. YASSINE, SYED M. MOIN, APRIL M. KILLIKELLY, GWO-YU CHUANG, ALIAKSANDR DRUZ, IVELIN S. GEORGIEV, EMILY J. RUNDLET, MALLIKA SASTRY, GUILLAUME B. E. STEWART-JONES, YONGPING YANG, BAOSHAN ZHANG, MARTHA C. NASON, CRISTINA CAPELLA, MARK E. PEEPLES, JULIE E. LEDGERWOOD, JASON S. MCLELLAN, PETER D. KWONG, AND BARNEY S. GRAHAM fewer Authors Info & Affiliations

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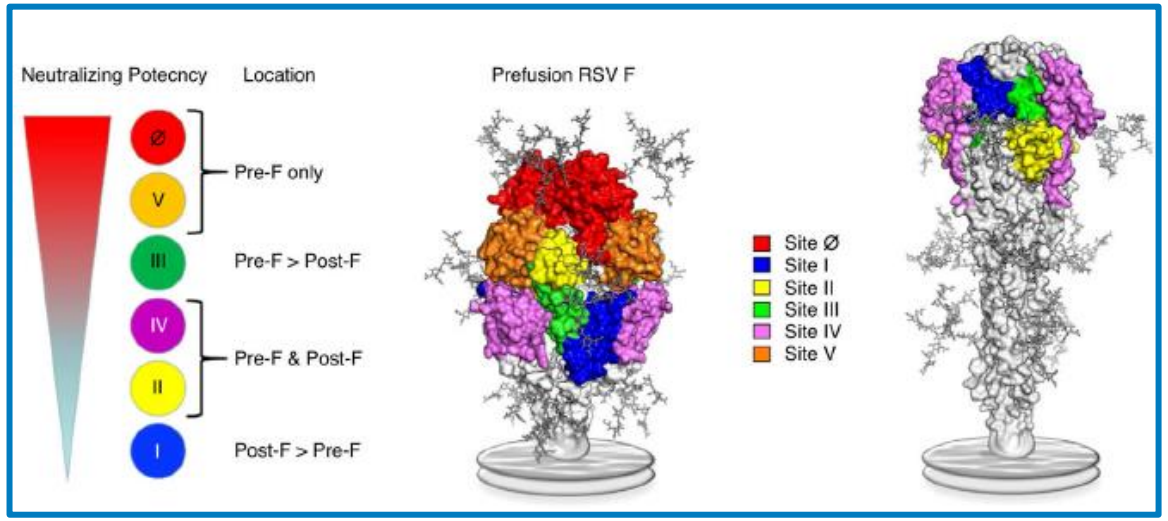
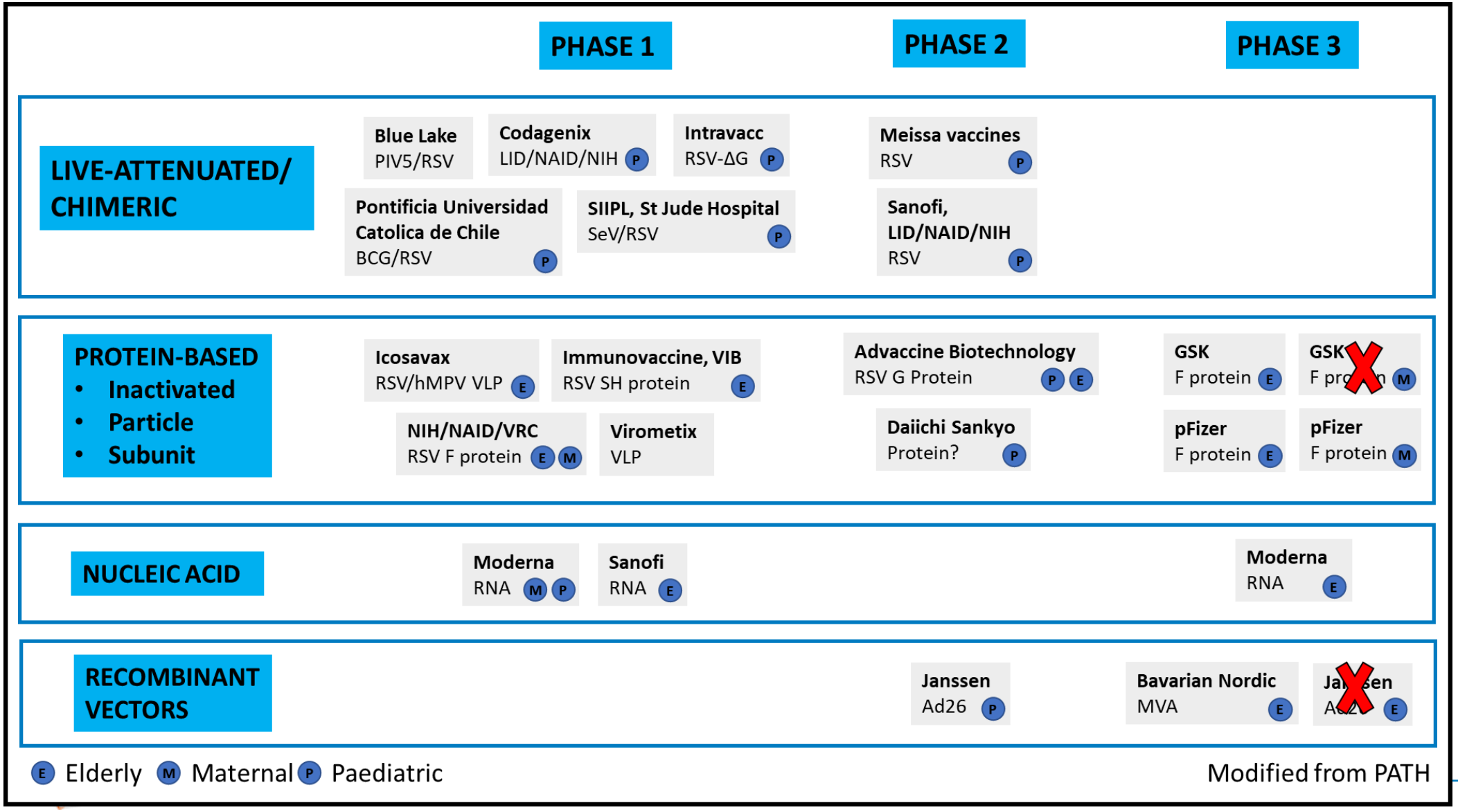
What does an mRNA RSV vaccine look like?

- PreF membrane-bound
- Delivered by mRNA LNP
- Nabs & Cellular immunity without Th2 skewing
- Maternal immunization followed by paediatric
- In line with WHO preferred product characteristics for RSV vaccine



Graham et al., 2015

Clinical pipeline for RSV vaccines



Afrigen's value proposition for RSV

1. Partnerships for end-to-end vaccine development
2. mRNA technology transfer programme driving access for LMICs
3. 2nd Generation technology promising lower cost
4. Formulation partnerships geared at improved temperature stability
5. Local production of drug substance and drug product
6. Strengthen biomanufacturing know-how in Africa
7. Harness the capacity & ecosystem for end-to-end manufacturing

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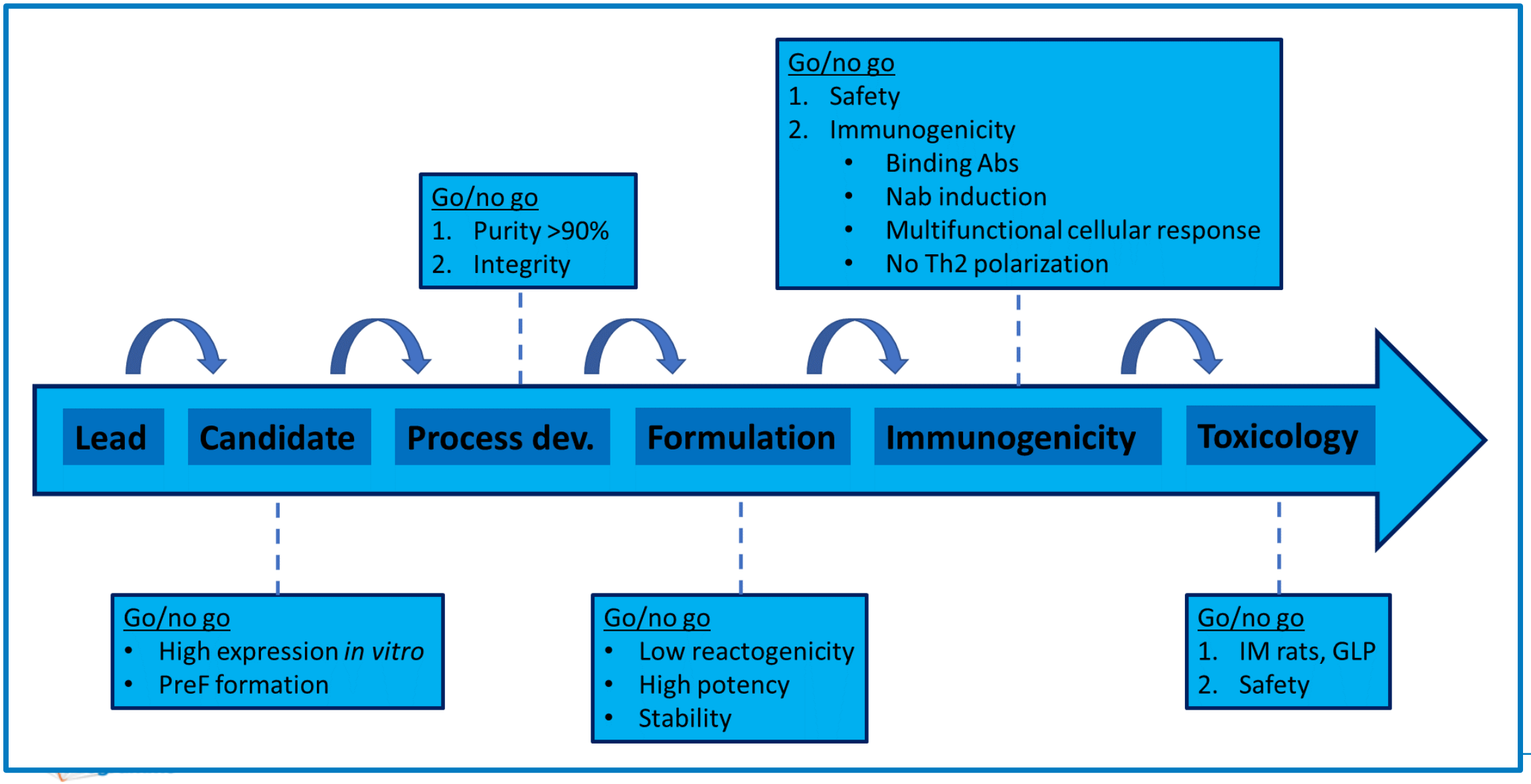
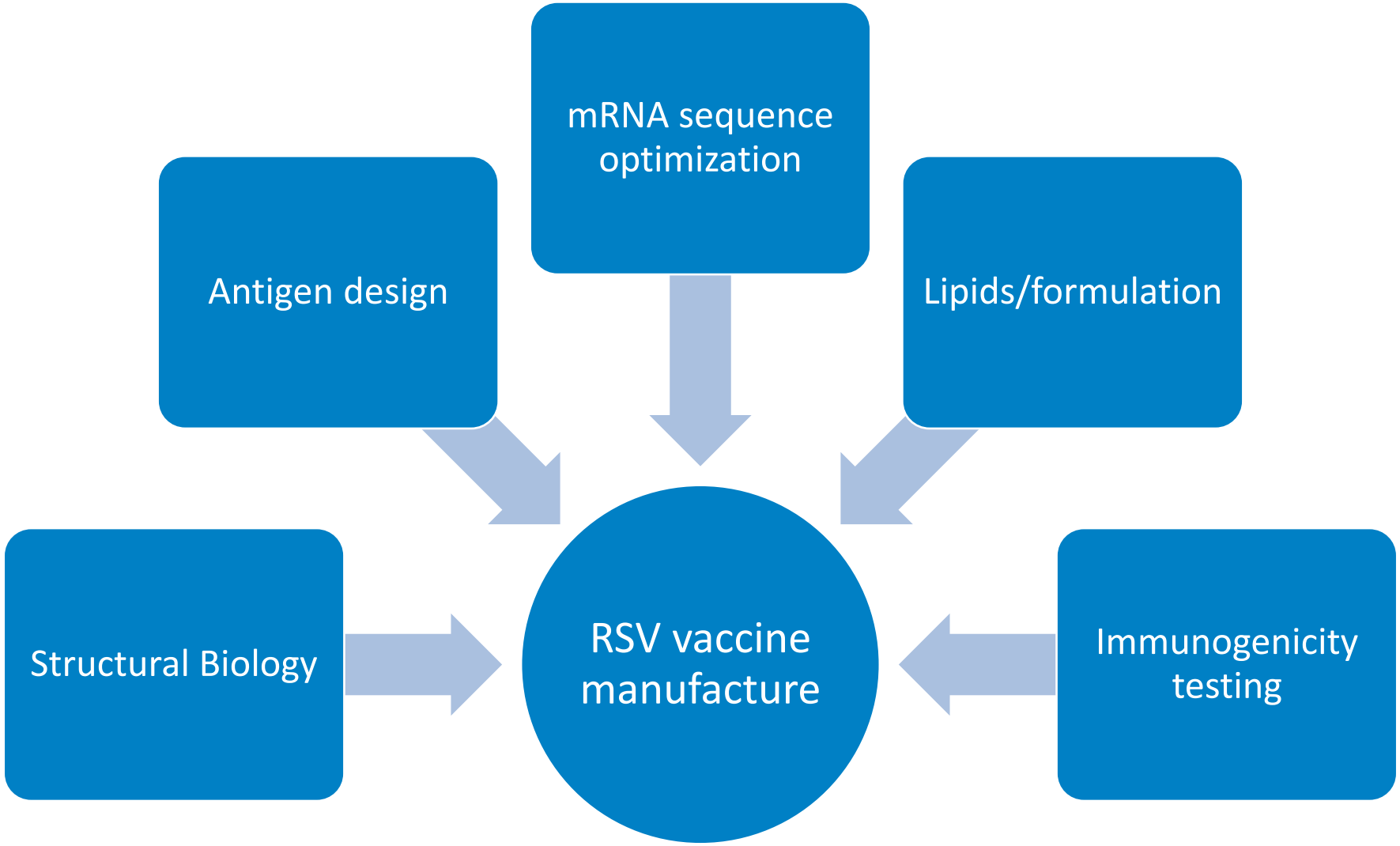
Preclinical development plan



Afrigen network for RSV



Summary

- High disease burden in Africa
- Likely lack of access to vaccine
- Well established concept for safe & effective vaccine
- Supported by clinical efficacy data (GSK, Pfizer, Moderna)
- Integration of novel UTRs & alternate lipids = freedom to operate
- Targeting refrigeration temperature stable formulations
- Establishing supporting network to commence experimental work

Acknowledgements

World Health Organization

medicines patent pool

Afrigen

NIH National Institutes of Health

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