



Søren Tetens Hoff

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Research Scientist

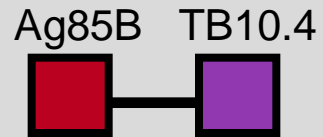
Department of Infectious Disease Immunology

Statens Serum Institut

Copenhagen, Denmark



HyVac4



Hybrid1

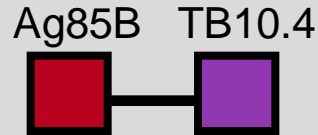


Hybrid56



Two different strategies / target populations

HyVac4



Boost an existing BCG-induced immunity

- Infants – children
- BCG vaccinated



Hybrid1



- Adolescents
- Regardless of BCG status or MTB infection status

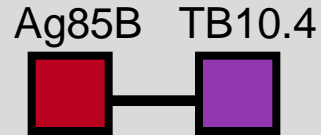


Hybrid56





HyVac4



IC31

Intercell

(KLK peptide +ODN1a)

Hybrid1



IC31

CAF01

SSI

(DDA+TDB)

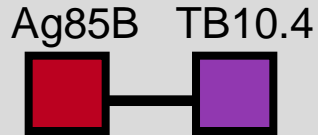
Hybrid56



IC31



HyVac4



IC31

Intercell

(KLK peptide +ODN1a)

Sanofi Pasteur

Aeras foundation

Hybrid1



IC31

CAF01

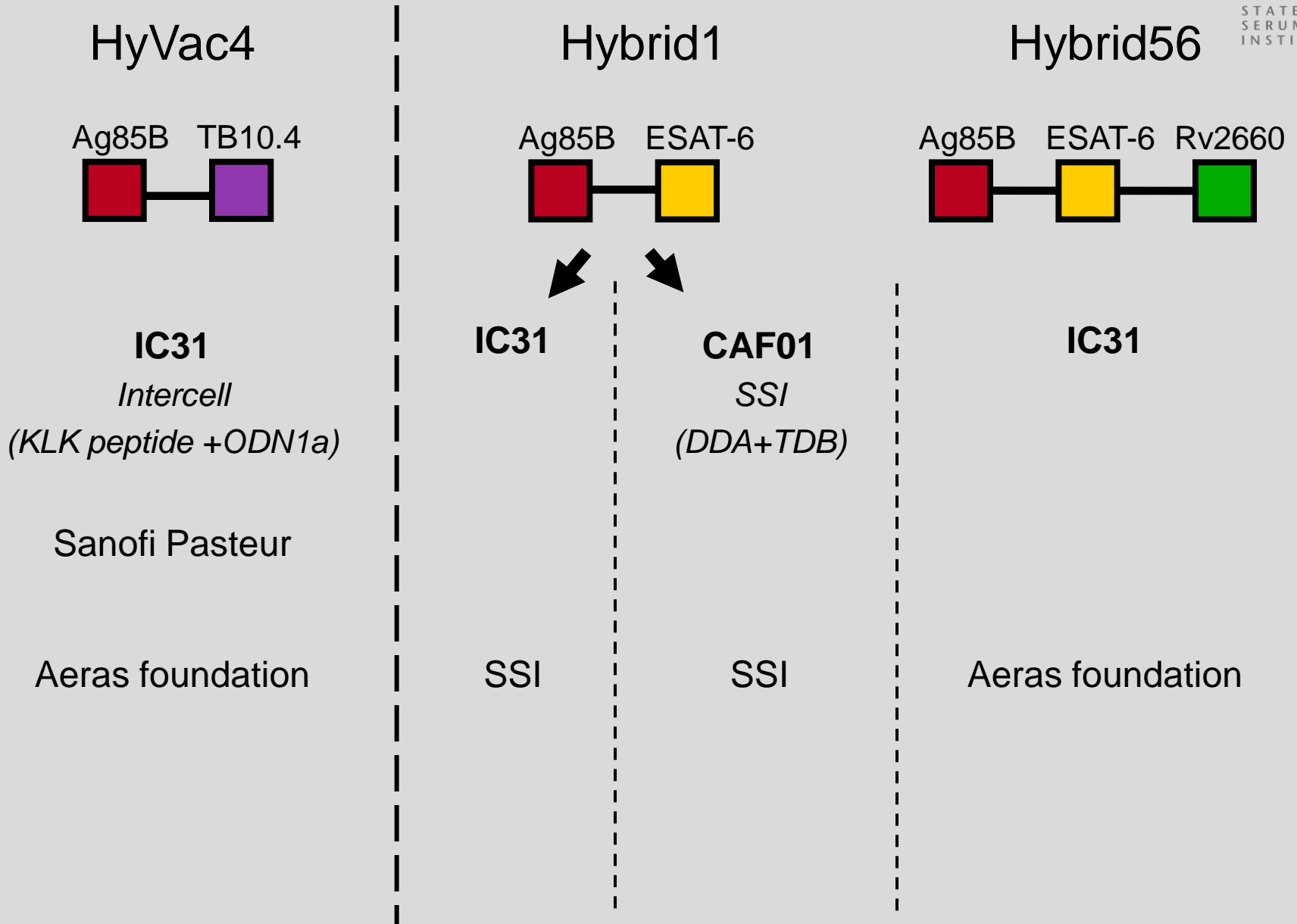
SSI

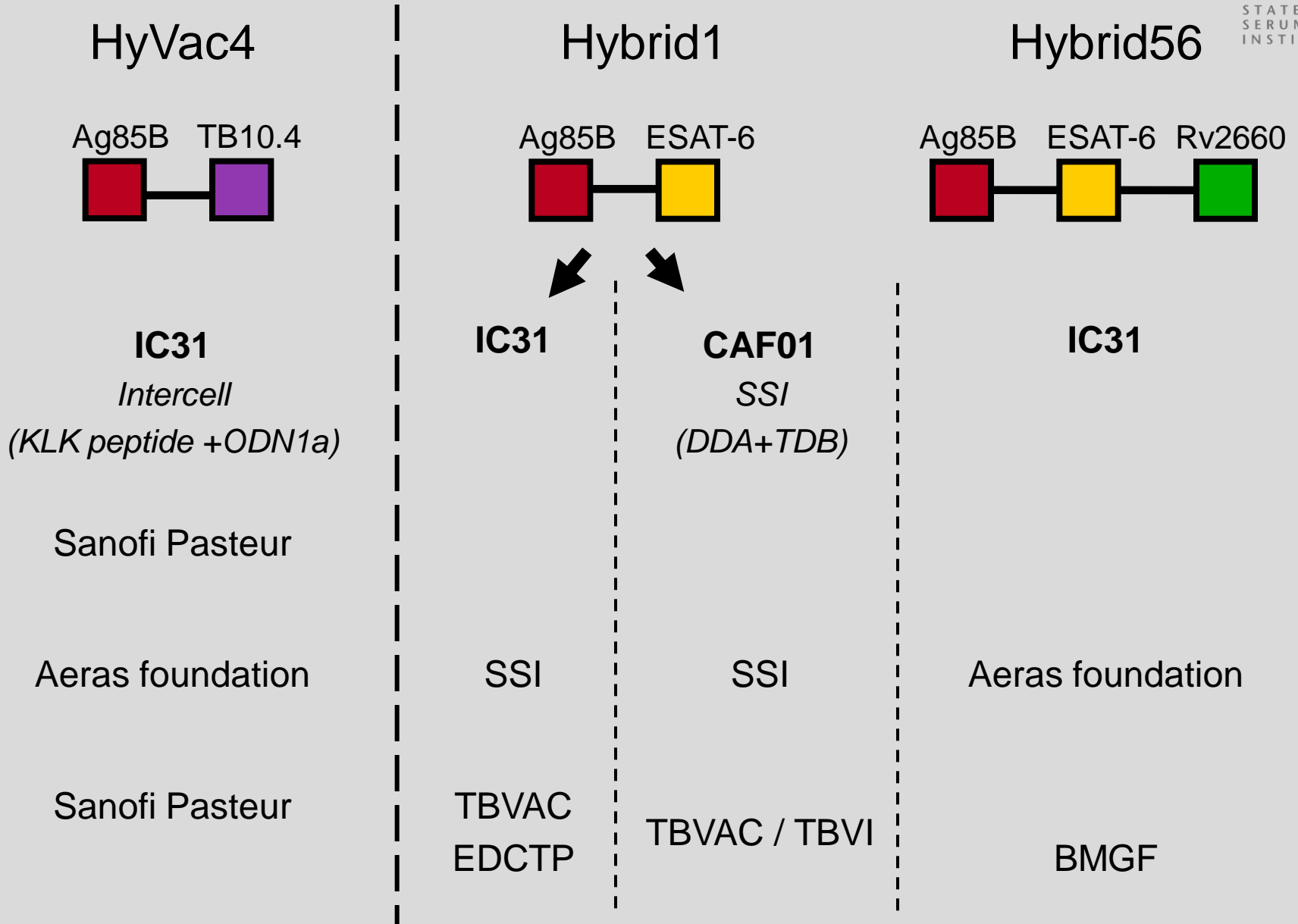
(DDA+TDB)

Hybrid56

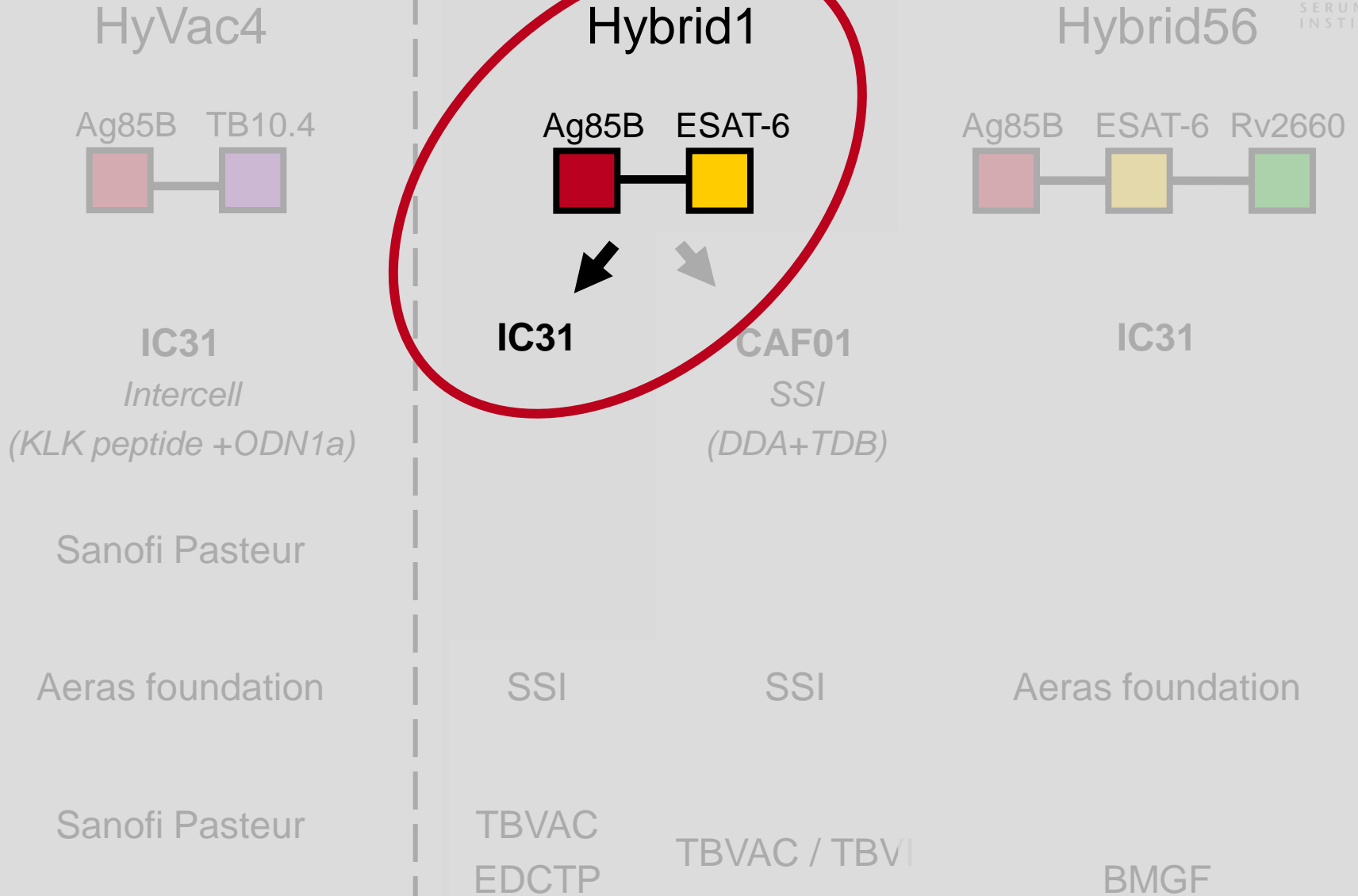


IC31

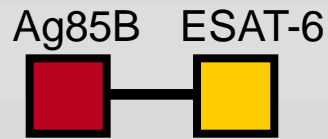




Clinical development



Hybrid1 (H1IC)



Trials: THYB-01/02: LUMC, The Netherlands

THYB-03: AHRI, Ethiopia (ongoing)

Objectives: Safety profile and immunogenicity in
different adjuvant regimens and different subject populations

Inclusion:

- BCG and MTB naïve individuals
- BCG vaccinated
- Prior MTB infection

Regimens:

H1: 50 ug (fixed)

IC-31: 0, 100 or 500 nmol

Schedule: 2 vaccinations (fixed)

Safety summary of THYB-01 and -02

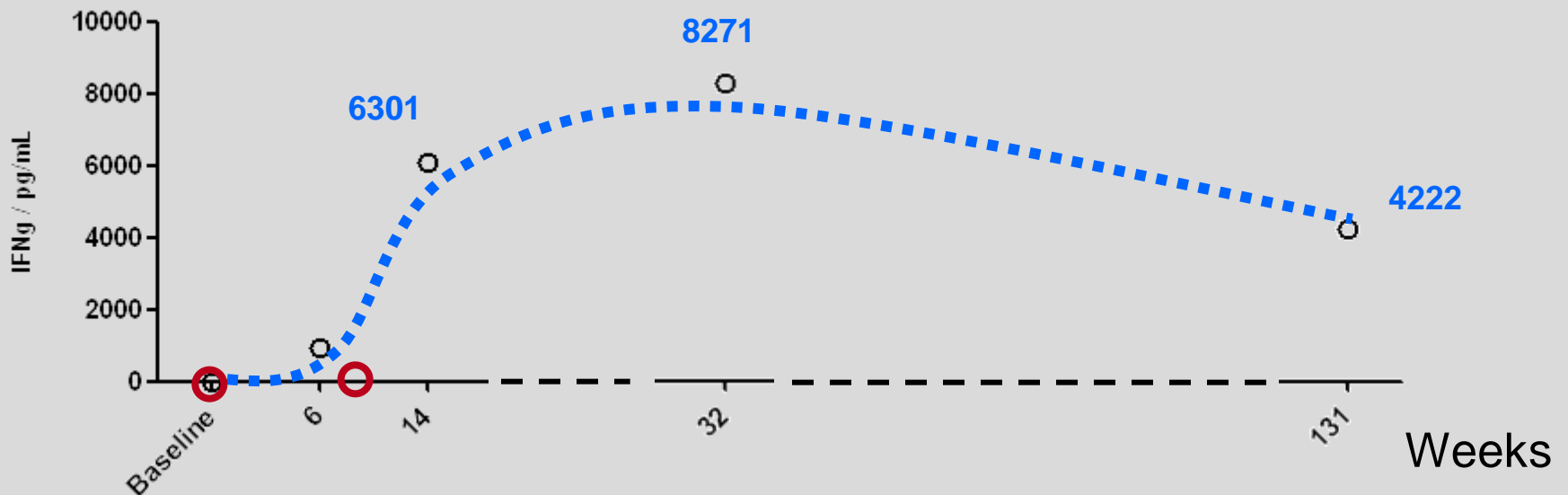
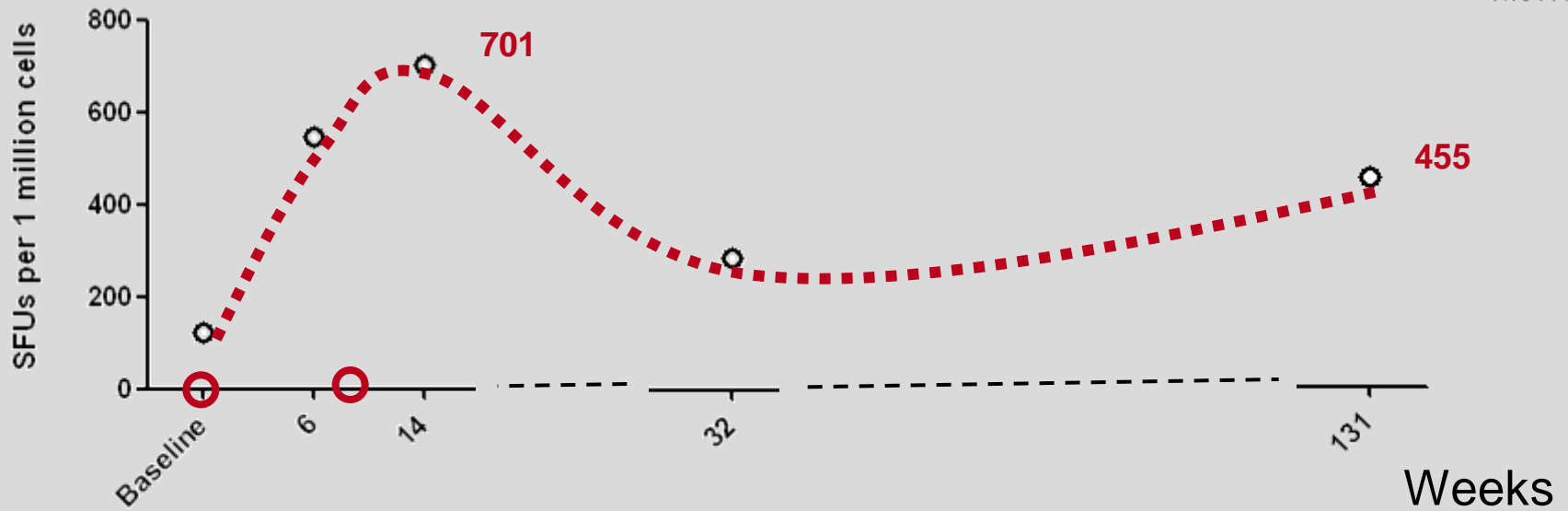
	Naïve THYB-01	BCG-vaccinated THYB-02	MTB- infected THYB-02
<i>Any local adverse event (n/N)</i>	10/11	8/10	9/10
Stiffness	5	4	5
Injection site pain	4	4	5
Bruising	1	3	0
Nodule	-	2	3
Skin irritation	-	3	8
<i>Any systemic adverse event (n/N)</i>	3/11	2/10	3/10
Fatigue	1	2	1
Pyrexia	1	-	-
Feeling feverish	-	-	2
Malaise	-	1	-
Infections	1	-	-

Immunogenicity THYB-01 and 02



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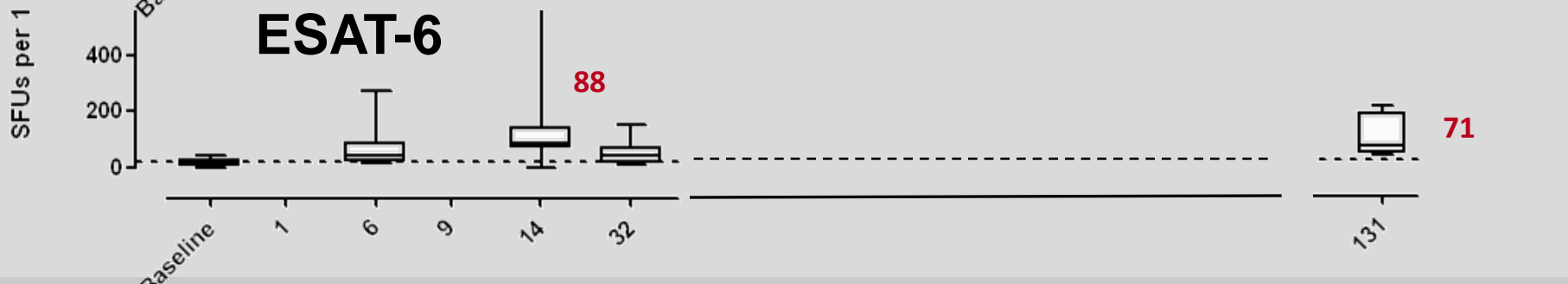
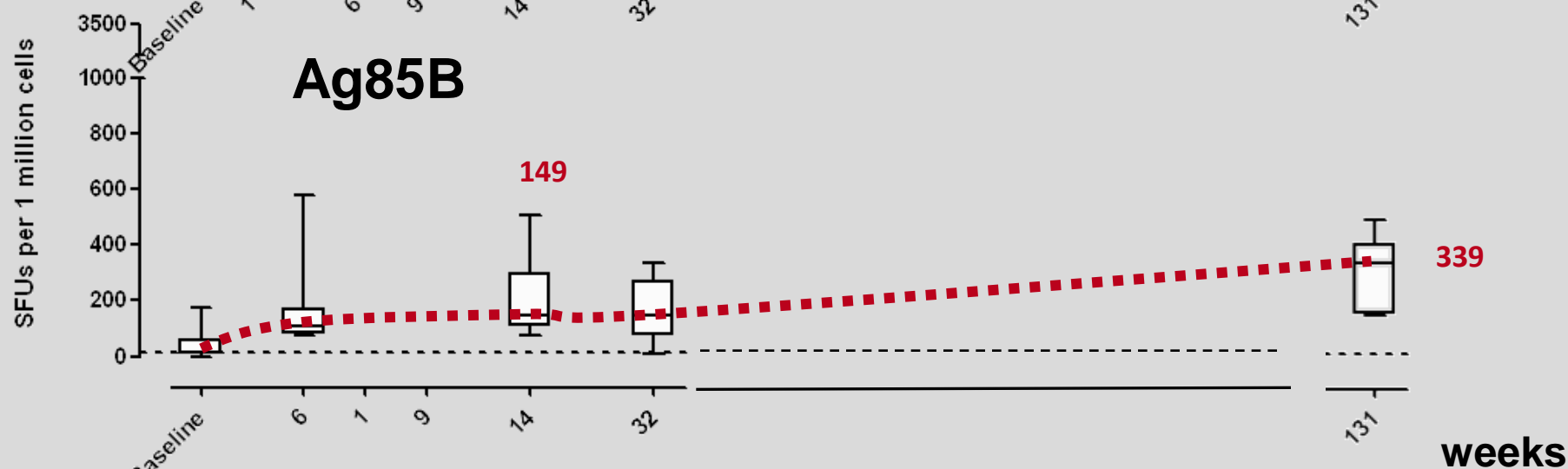
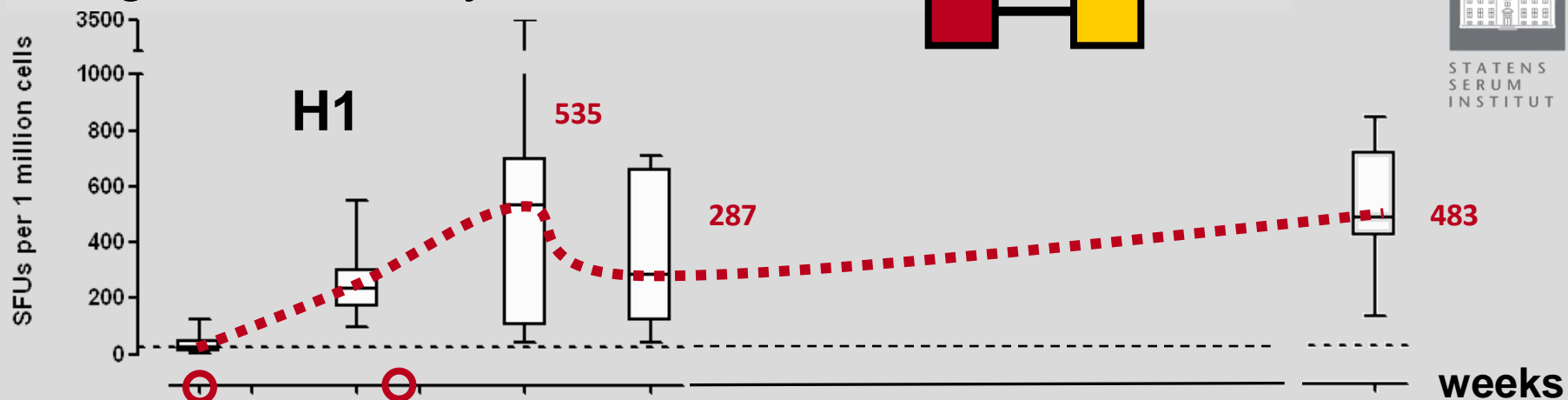
Data from one single Naïve donor



Long term memory in BCG naïve...



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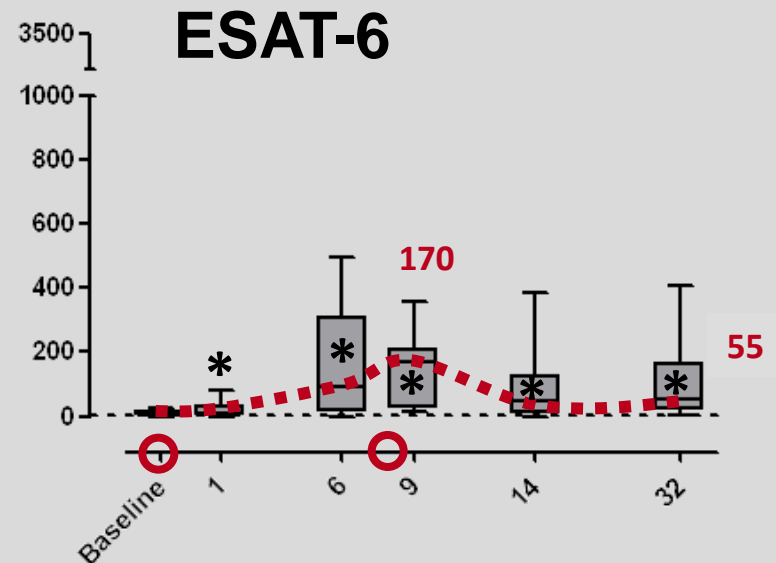
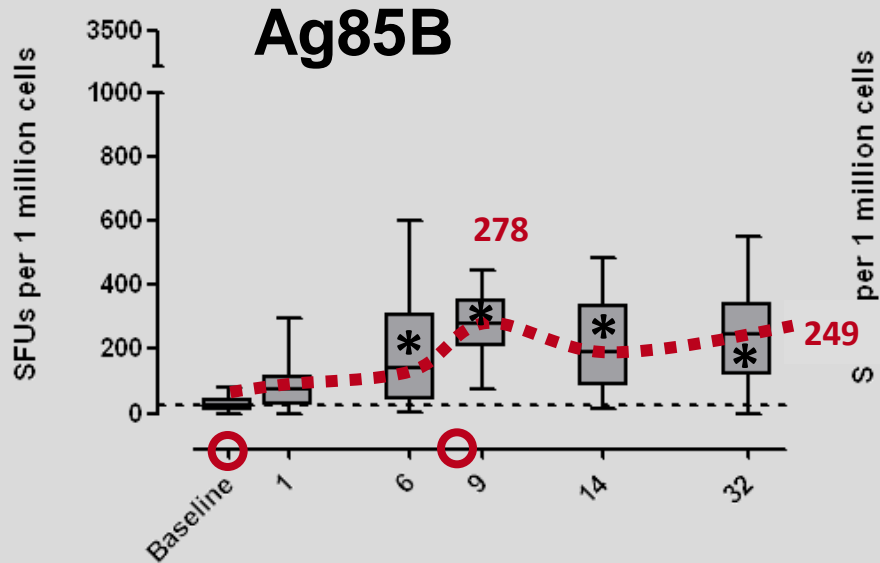
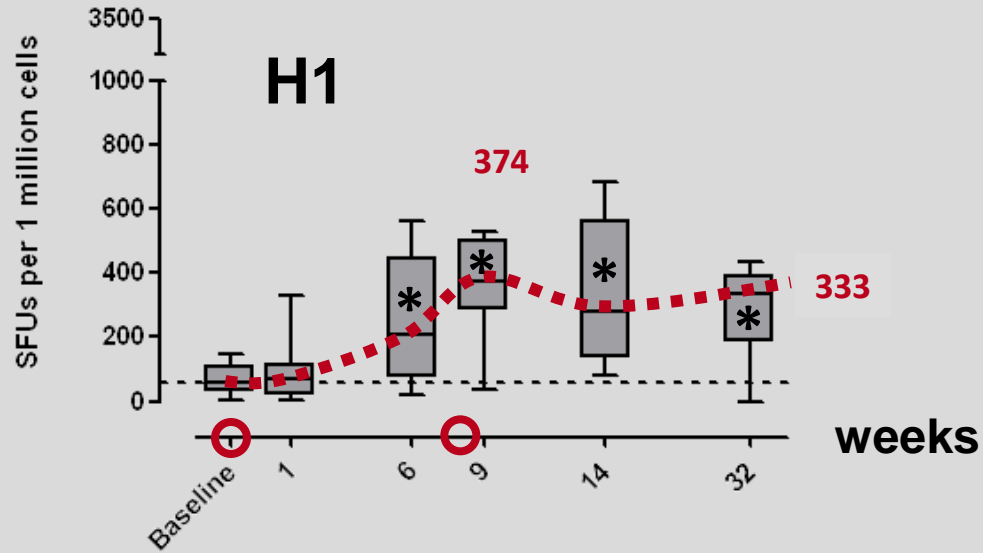


... BCG vaccinated

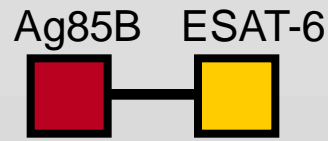
Ag85B ESAT-6



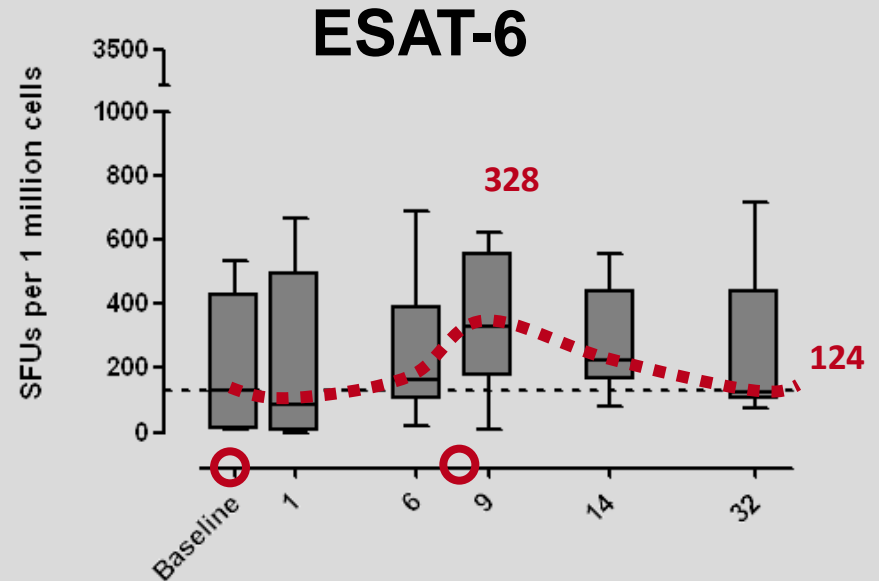
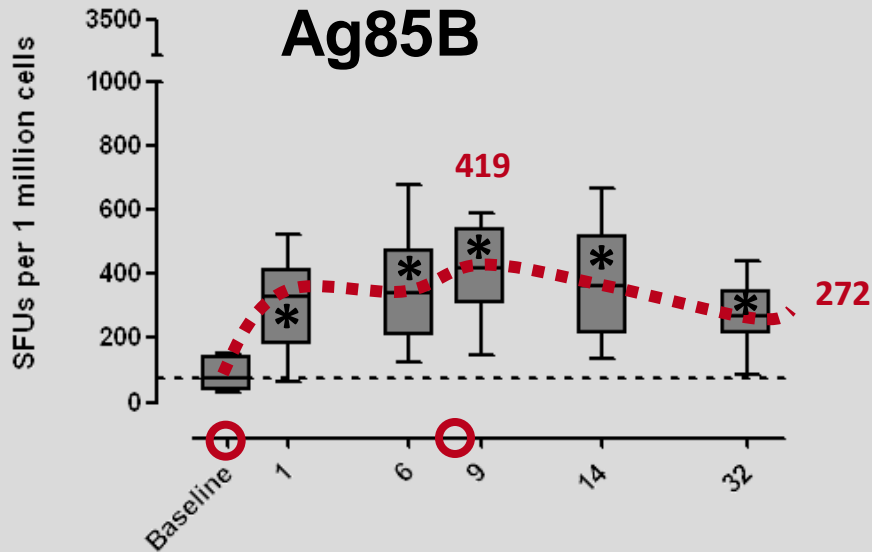
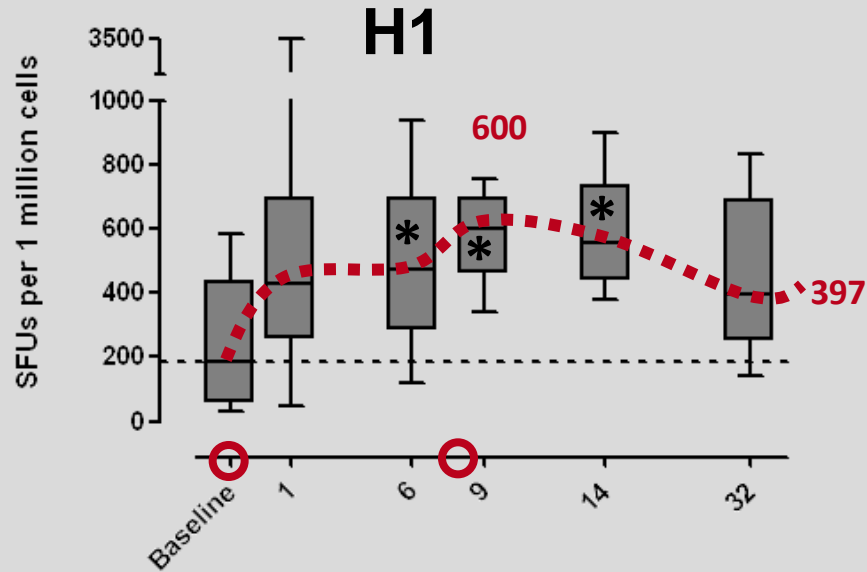
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...and prior MTB infected



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Hybrid1 (H1IC)



Trials: THYB-01/02: LUMC, The Netherlands
THYB-03: AHRI, Ethiopia (ongoing)

Objectives: Safety profile and immunogenicity in
different adjuvant regimens and different subject populations

Inclusion:

- BCG and MTB naïve individuals
- BCG vaccinated
- Prior MTB infection

Regimens: H1: 50 ug (fixed)
IC-31: 0, 100 or 500 nmol
Schedule: 2 vaccinations (fixed)

In planning: Phase II trial investigating antigen dose (15 or 50 ug) and
schedule (1 or 2 vaccinations)

SSI fusion molecules

HyVac4

Ag85B TB10.4



IC31

Intercell

(KLK peptide +ODN1a)

Sanofi Pasteur

Aeras foundation

Sanofi Pasteur

Hybrid1

Ag85B ESAT-6



IC31

CAF01

SSI

(DDA+TDB)

Hybrid56

Ag85B ESAT-6 Rv2660



IC31

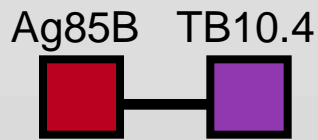
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BMGF

TBVAC
EDCTP

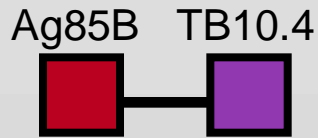
TBVAC / TBVI

HyVac4 (Aeras-404)



- Trials:**
- | | |
|-----------|---------------------|
| C005-404: | Karolinska, Sweden |
| C006-404: | Tampere, Finland |
| C011-404: | Satvi, South Africa |
- Objectives:** Safety profile and immunogenicity of **different antigen/adjuvant regimens**
- Inclusion:** BCG-vaccinated healthy volunteers
- Regimens:**
- | | |
|-----------|---------------------|
| HyVac4: | 5, 15, 50 or 150 ug |
| IC31: | 0, 100 or 500 nmol |
| Schedule: | 1 or 2 vaccinations |
- Primary Imm. measure:** ICS Flow cytometry and IFN γ ELISPOT

HyVac4 (Aeras-404)



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Preliminary safety and immunogenicity:

- Acceptable safety profile
 - Local reactions at sites of recent (but not remote) tuberculin skin tests
- HyVac4 and H1IC have yielded comparable immunogenicity results as measured by IFN γ ELISPOT in similar populations

HyVac4 (Aeras-404)

Ag85B TB10.4



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Trials: C005-404: Karolinska, Sweden
C006-404: Tampere, Finland
C011-404: Satvi, South Africa

Objectives: Safety profile and immunogenicity of
different antigen/adjuvant regimens

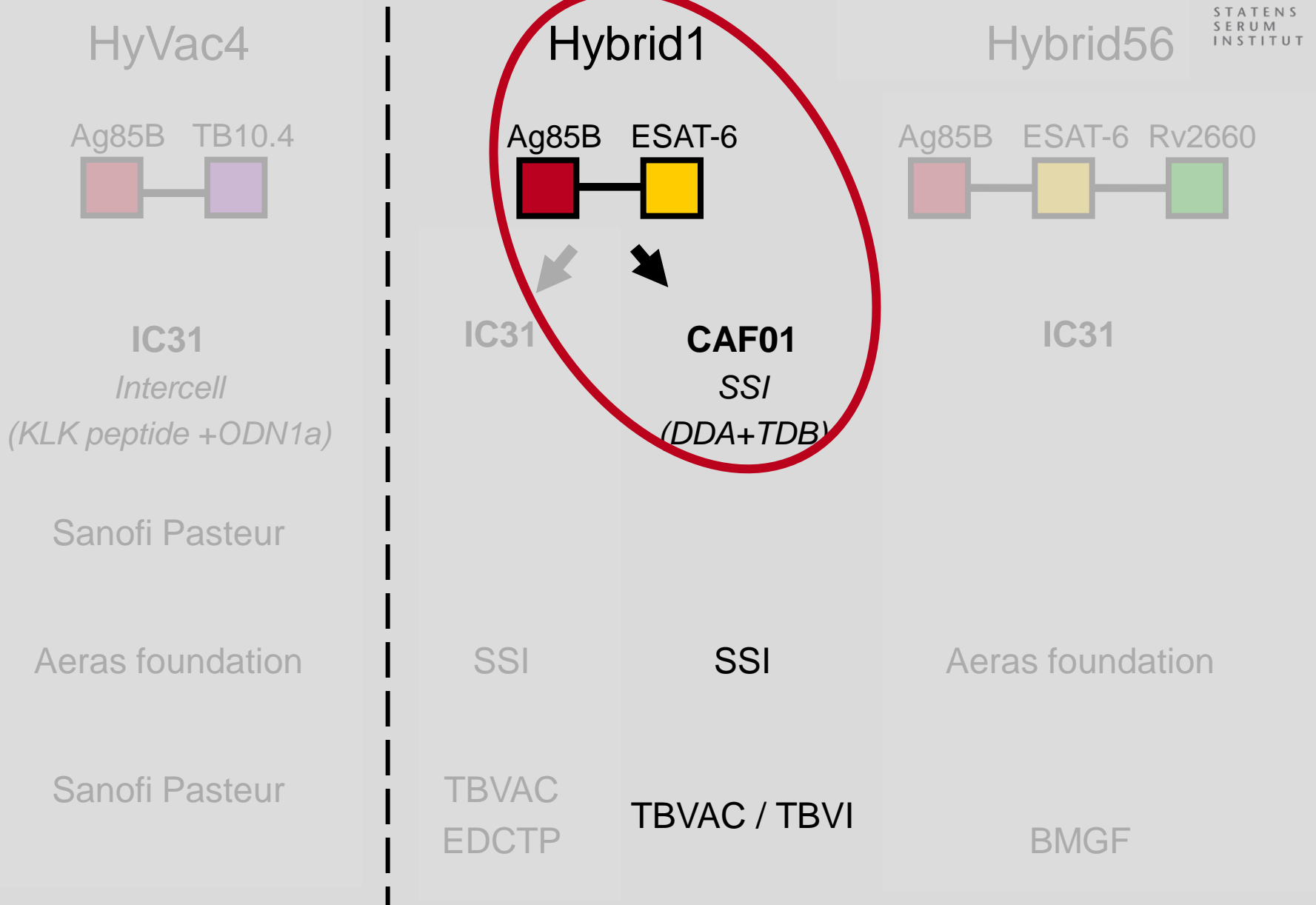
Inclusion: BCG-vaccinated healthy volunteers

Regimens: HyVac4: 5, 15, 50 or 150 ug
IC31: 0, 100 or 500 nmol
Schedule: 1 or 2 vaccinations

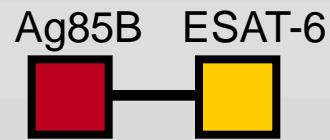
Primary Imm. measure: ICS Flow cytometry and IFN γ ELISPOT

In planning: Proximal BCG prime-boost in adults, toddlers and infants
Phase II proof-of-concept

SSI fusion molecules



Hybrid1 (H1-CAF01)



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Trials: ACAF01-01: The Netherlands

Objectives: Safety profile of **different adjuvant regimens**
Assessment of immunogenicity profile

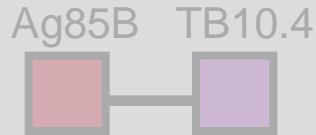
Inclusion: 37 healthy BCG and MTB naïve volunteers

Regimens: H1: 50 ug (fixed)
CAF01 (DDA/TDB): **0, 125/25, 313/63 or 625/125 ug**
Schedule: 2 vaccinations (fixed)

Primary Imm. measure: IFN γ ELISPOT and IFN γ ELISA

SSI fusion molecules

HyVac4



IC31

Intercell

(KLK peptide +ODN1a)

Sanofi Pasteur

Aeras foundation

Sanofi Pasteur

Hybrid1



IC31

CAF01

SSI

(DDA+TDB)

SSI

SSI

TBVAC
EDCTP

TBVAC / TBVI

Hybrid56



IC31

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BMGF

Hybrid56 (H56IC / Aeras-456)



Trials: C032-456: (in planning)

Objectives: Safety profile and immunogenicity of
different regimens and different populations

Inclusion: Healthy volunteers with either no history of MTB infection
or known latent MTB infection

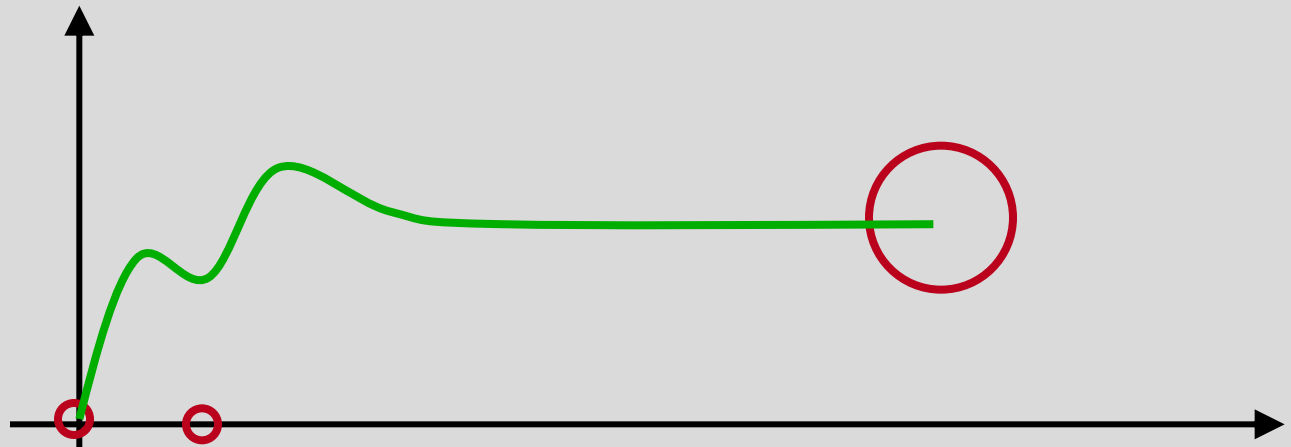
Regimens:

H56:	5, 15 or 50 ug
IC31:	500 nmol (fixed)
Schedule:	2 vaccinations (fixed)

Primary Imm. measure: ICS Flow cytometry and IFN γ ELISPOT

Conclusions

- *SSI TB subunit vaccines have until now shown to be safe and well tolerated in different populations and with different regimens*
- *The vaccines are clearly immunogenic generally showing a bi-modal response curve with peak responses after the 2nd vaccination*
- *H1IC has shown to induce a long-term (2.5 years) memory response to the vaccine of more than 400 SFUs above baseline - also in BCG naïve subjects*
- *These vaccines may share the ability to induce immunity even in non-BCG primed individuals*



Thanks



SSI

Department of Infectious Disease
Immunology

Vaccine development department SSI

Quality Control
Quality Assurance
Regulatory Affairs
Fill and Finish

External collaborators

Sanofi pasteur
Aeras foundation
Intercell
LUMC
AHRI
Satvi
Karolinska institutet
University of Tampere
CHUV
TBVI / TBVAC
Bill and Melinda Gates foundation
EDCTP



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sanofi pasteur

La division vaccins du Groupe sanofi-aventis.



AERASSM
GLOBAL TB VACCINE FOUNDATION

