Spring 5-24-2012

Flunisyn: Advanced development of a synthetic universal influenza t-cell vaccine

Campbell Bunce
ITS ltd

IMMUNE TARGETING SYSTEMS

Flunisyn: Advanced Development of a Synthetic Universal Influenza T-cell Vaccine

Vaccine Technology IV
Albufeira, Portugal

24th May 2012

Disclaimer

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Immune Targeting Systems

London based biotech company developing vaccines for mutating viruses and cancer

Lead Program: Universal Flu vaccine (Flunisyn™)

- 2nd Phase-I study complete (Flunisyn +/- Adjuvant) - Phase 2a initiation H2-2012
- Existing flu vaccines – poorly effective & don't deliver T-cell correlates of protection

Pipeline extension offers unique targeted product profiles

- Universal Hepatitis B therapeutic vaccine – targets antiviral treatment cessation (7MM/Asia)
- Cancer vaccine platform – Maximising immunogenicity whilst eliminating HLA screening

Investors:

NOVARTIS Venture Fund · HealthCap · Truffle Capital · ESPERANTE VENTURES · LF

Mutating Viruses: Disease protection requires T-cell immunity

Performance Parameter	Benefit	Flunisyn™
Re-use capability (Booster effect) *	Single vaccine regimen (Avoids heterologous prime-boost strategy)	✓
Responder frequency	High % respond to vaccination (Eliminates HLA typing of human subjects)	✓
Breadth of response	Improved antiviral activity	✓
Magnitude & Quality of response	Improved antiviral activity	✓
Broad cross reactive T-cell immunity	All viral strains / genotypes	✓

Historical T-cell vaccine pipeline failures highlight rate limiting immunological performance parameters

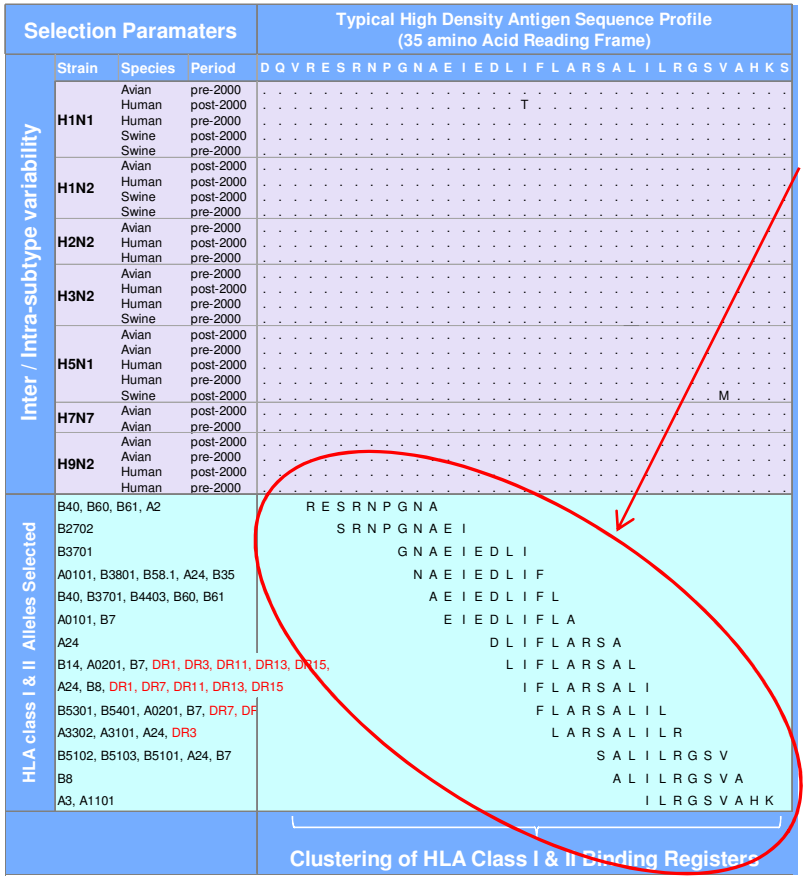
Improved vaccines must address full correlates of protection (unachieved by adjuvants alone)

DepoVaccine™ Promotes a Short Term Antigen Depot

DepoVaccines promote an antigen depot (↑ $T_{1/2}$)

Depot forming adjuvant boosts immunogenicity

Synthetic: Scalable, Stable & Characterisable



DepoVaccine™ Antigen Delivery System

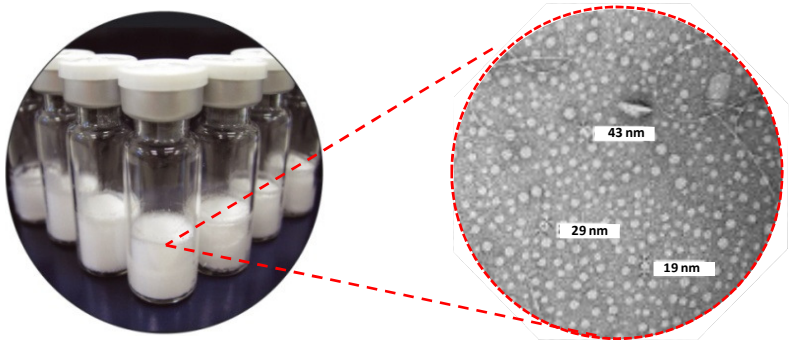
Densigen™

- 35aa conserved immunoprevalent antigen
- Non-envelop viral protein hydrophobic cores

PB1/2, PA, NP & M1 viral antigens

Freeze Dried Nanoparticle Formulation

Flunisyn – contains 6 different Densigens



Cryotransmission EM of Flunisyn formulation

Flunisyn™: First Time in Human Study

Objective: Dose escalation study to establish initial data set with prototype formulation of Flunisyn (non-adjuvanted) – double blind and placebo controlled

1. Safety & immunogenicity (dose response)
2. Quality of immune response
   a) T cell phenotype (cytokine expression, CD4/CD8)
   b) X-reactivity to disparate influenza strains

Study design:

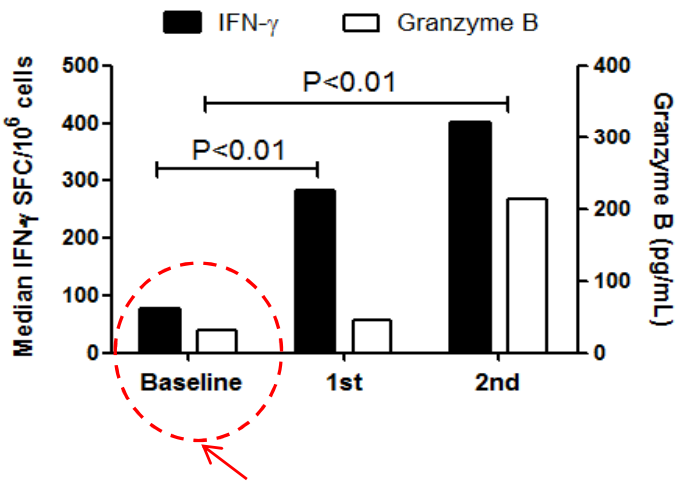
Group (n = 12 per cohort)	Injections	Blood samples
Placebo	Day 1, 29 & 99	Day -7. 1, 8, 15, 29, 36, 53, 99, 106, 113, 279
Flunisyn (50µg/peptide)	Day 1, 29 & 99	Day -7. 1, 8, 15, 29, 36, 53, 99, 106, 113, 279
Flunisyn (150µg/peptide)	Day 1, 29 & 99	Day -7. 1, 8, 15, 29, 36, 53, 99, 106, 113, 279
Flunisyn (500µg/peptide)	Day 1, 29 & 99	Day -7. 1, 8, 15, 29, 36, 53, 99, 106, 113, 279

Flunisyn™ Phase-I Clinical Summary

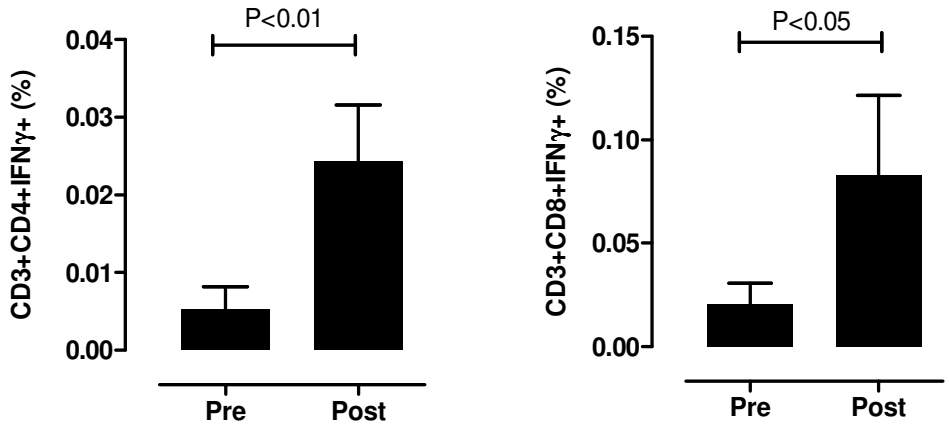
Flunisyn is safe and well tolerated at all doses tested

Immunogenicity:

Magnitude & booster amplification



Increases in both CD4+ and CD8+ T cells post vaccination (day 36)



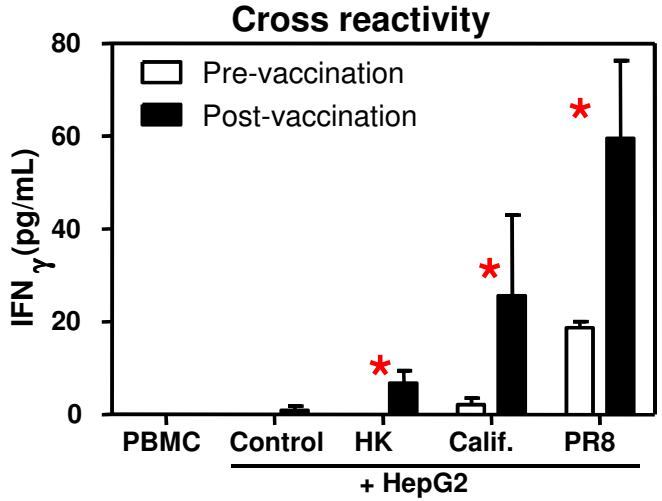
Flunisyn-specific T cell response (n=11)
measured by intracellular cytokine staining

Flunisyn™ Phase-I Clinical Summary (*cont.)*

No difference in HLA-restriction between vaccine responders and overall HLA prevalence

HLA-supertype	Responder		Overall Prevalence
	n / 21	%	%
HLA-A01	8	38%	52%
HLA-A02	11	52%	48%
HLA-A03	12	57%	45%
HLA-A24	2	10%	15%
HLA-B07	14	67%	55%
HLA-B08	3	14%	24%
HLA-B27	4	19%	15%
HLA-B44	8	38%	42%
HLA-B58	3	14%	21%
HLA-B62	1	5%	6%
HLA-DR1	5	24%	24%
HLA-DR3	4	19%	24%
HLA-DR4	2	10%	12%
HLA-DR7	7	33%	30%
HLA-DR11	4	19%	15%
HLA-DR13	4	19%	15%
HLA-DR15	5	24%	21%

Flunisyn specific T-cells recognise cells infected with different influenza A virus strains



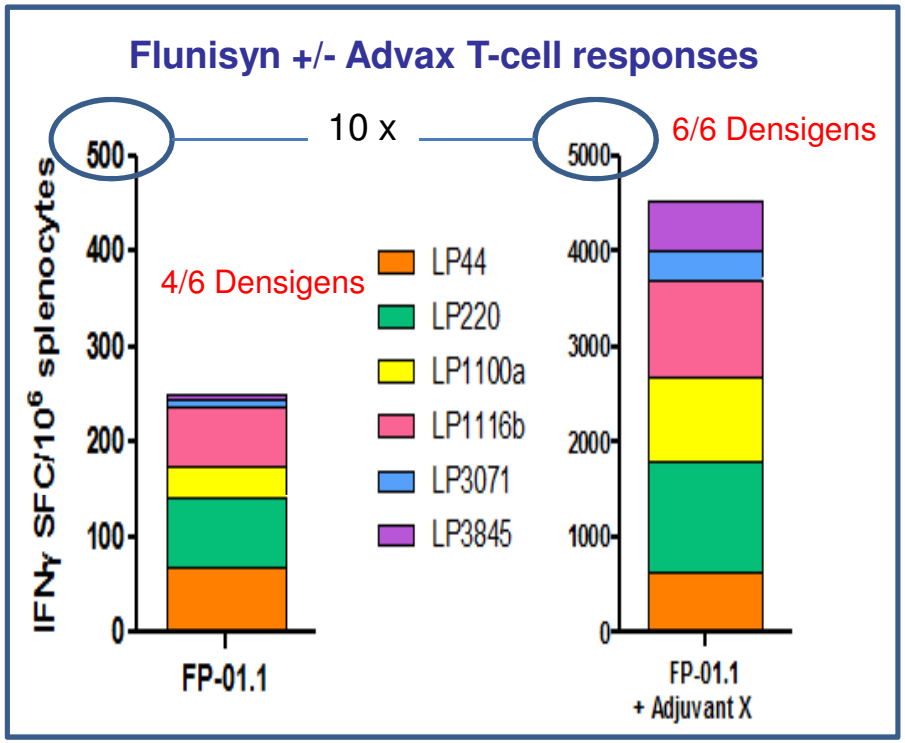
* Cross-reactivity correlated with degree of hepatoma cell line infectivity

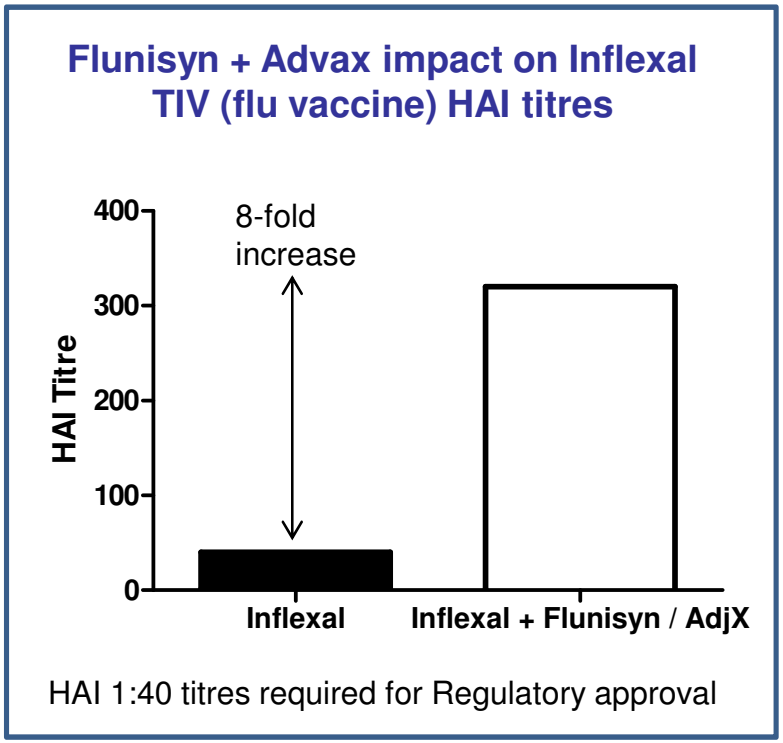
Flunisyn™: Key Performance Parameters

Immunologically optimum dose – highlights its best-in-class potential:

- ✓ **Responder frequency: 10/12 subjects met responder criteria (without HLA screening)**
- ✓ **Booster amplification: confirmed (at 1st & 2nd booster)**
- ✓ **Breadth: mean 4.5 / 6 antigens (incl. multi-epitopic CD4 & 8 / antigen)**
- ✓ **Magnitude: significant increase over base line**
- ✓ **Cross reactivity: all potential seasonal & pandemic flu strains**

Advax Significantly Enhances T-cell Immunogenicity (non Clinical)

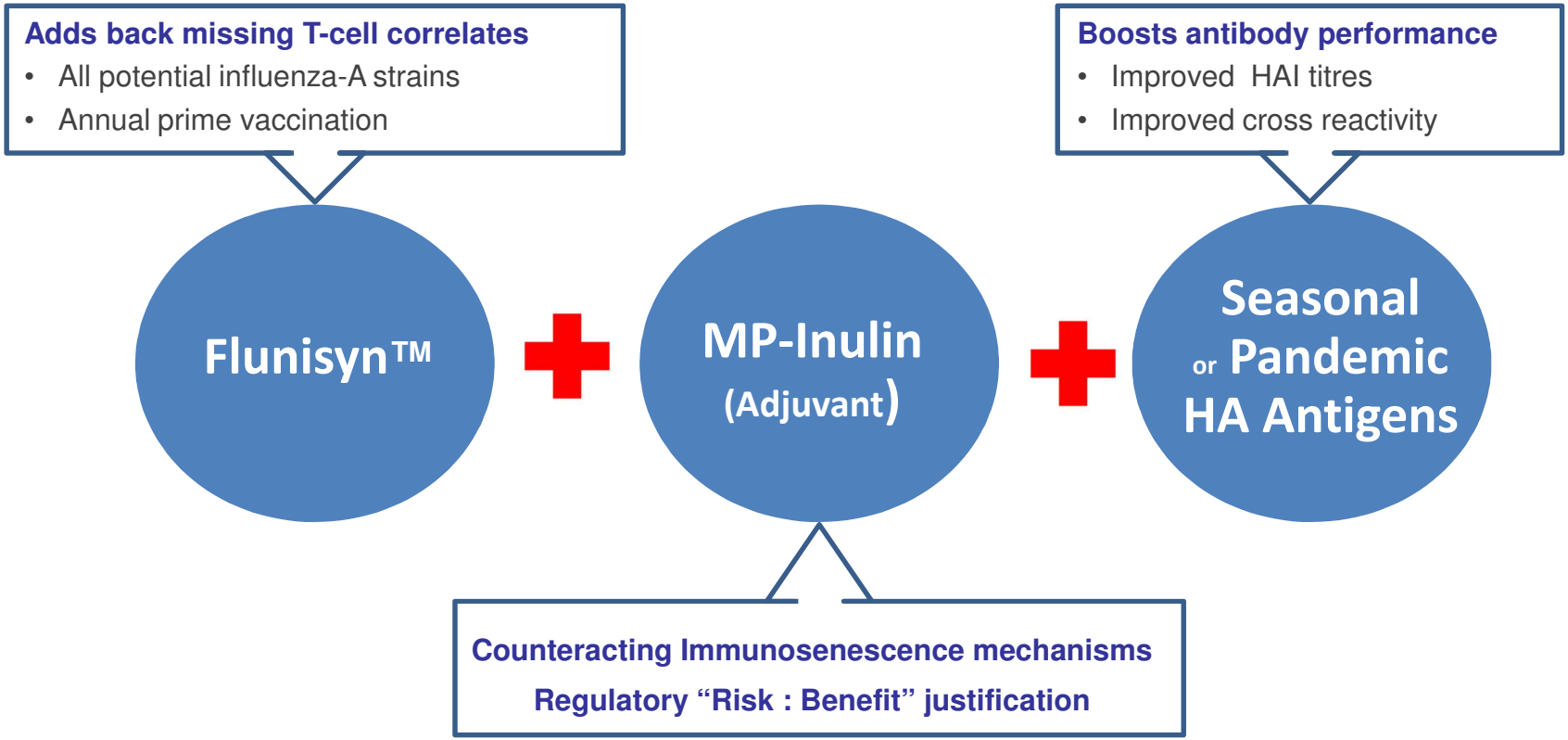




Advax (microparticulate Inulin) enhances Flunisyn & functional antibody responses to hemagglutinin (Rats)

- Magnitude of response (20X)
- Breadth of response (>50% include multi-epitopic / peptide responses)
- CD8 profile (30-40% of total response)
- Antiviral cytokines (500X)
- HAI antibody titres (8X or 1:320)

Improved Influenza Disease Protection



Lead indication: Improved Elderly seasonal flu vaccine – Flunisyn / MP-Inulin + TIV

Established seroprotection surrogate end-points are not correlated with clinical disease protection

- Clinical studies highlight T-cell immunity drives influenza disease protection
- Current seasonal flu vaccine does not deliver T-cell immunity

Developing Unique Products and Platform

Flunisyn Programme:

- Start First in Elderly study Q2 2012
- Live virus challenge study H1 2013

Universal Hepatitis B vaccine (Hepsyn) Programme:

- Pre-clinical GxP 2012/2013
- Phase 1b H2 2013

Oncology Programme:

- PoC Q3 2012
- Target selection Q3 2012