



HSV-2 Phase IIa results
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Wayne Paterson
CEO
Admedus

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Presentation Summary

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- Introduction
- Study overview
- Phase IIa results
- Study conclusions
- Next steps
- Immuno-oncology programs
- Summary



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Introduction



- RNA & DNA therapeutic development Company
- Based around core technology initially developed by Prof Frazer
- Core IP covering ubiquitin with optimised RNA/DNA

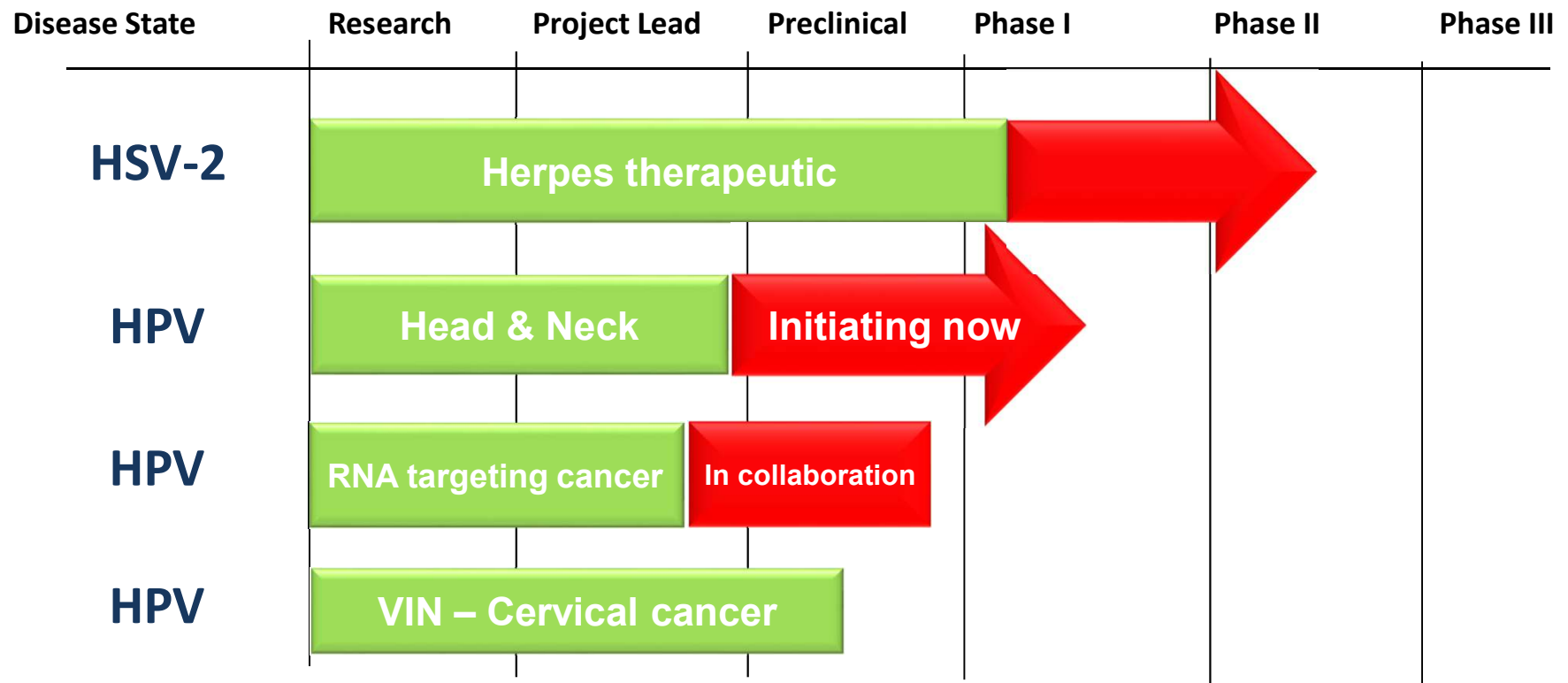


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Company pipeline



Target diseases



| Program | Target Market Size |
|--|--|
| RNA immuno-oncology | Multiple oncology applications |
| HPV Head & Neck in combination with checkpoint inhibitor | 85,000 new cases p.a. HPV related cases rapidly increasing |
| HPV VIN patients | 7 cases per 100,000 women pa Fourfold increase in cases between 1973 and 2000 |
| HSV-2 | 490 million people infected No effective vaccine on market |



Herpes simplex 2

HSV-2 Phase I study summary



The HSV-2 Vaccine has 3 components

- **COR-1A: plasmid DNA coding for optimized glycoprotein D, surface protein of HSV-2 (gD2)**
- **COR-1B: plasmid DNA coding optimized gD2 fused to ubiquitin**
- **Buffering solution**
- **Plasmids formulated in 1:1 ratio with the buffer solution**
- **Manufactured under cGMP by VGXI, Texas USA**
- **Stored frozen at -20C in 2ml vial**
- **Delivered by standard needle and syringe by intradermal injection**
- **No additional adjuvant added**



HSV-2 Phase I study summary

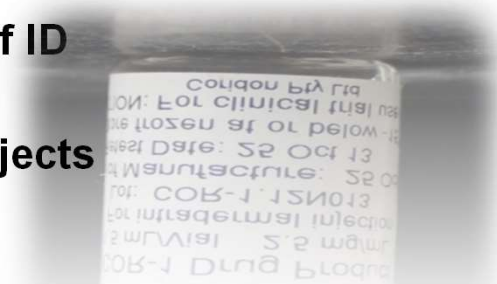
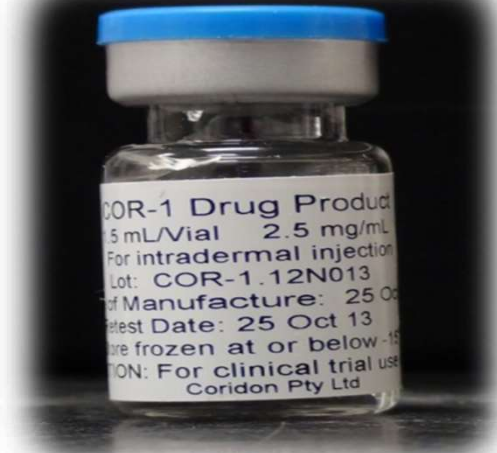


Phase I study design

- Safety, Tolerability & Immunogenicity Endpoints
- Open Label, Dose Escalation
- 20 healthy sero-negative 18 - 45 yrs old subjects
- Doses: 10µg, 30µg, 100µg, 300µg, & 1mg (2 x 500 µg)
- Intradermal injections (Days 0, 21 and 42)
- 3 week EOS visit after 3rd dose

Phase I results

- Study achieved primary endpoint for safety and tolerability of ID injection
- Results showed T-cell responses in 95% (19 of 20) study subjects
- Local DTH reactions clearly dose dependent



HSV-2 Phase IIa study summary



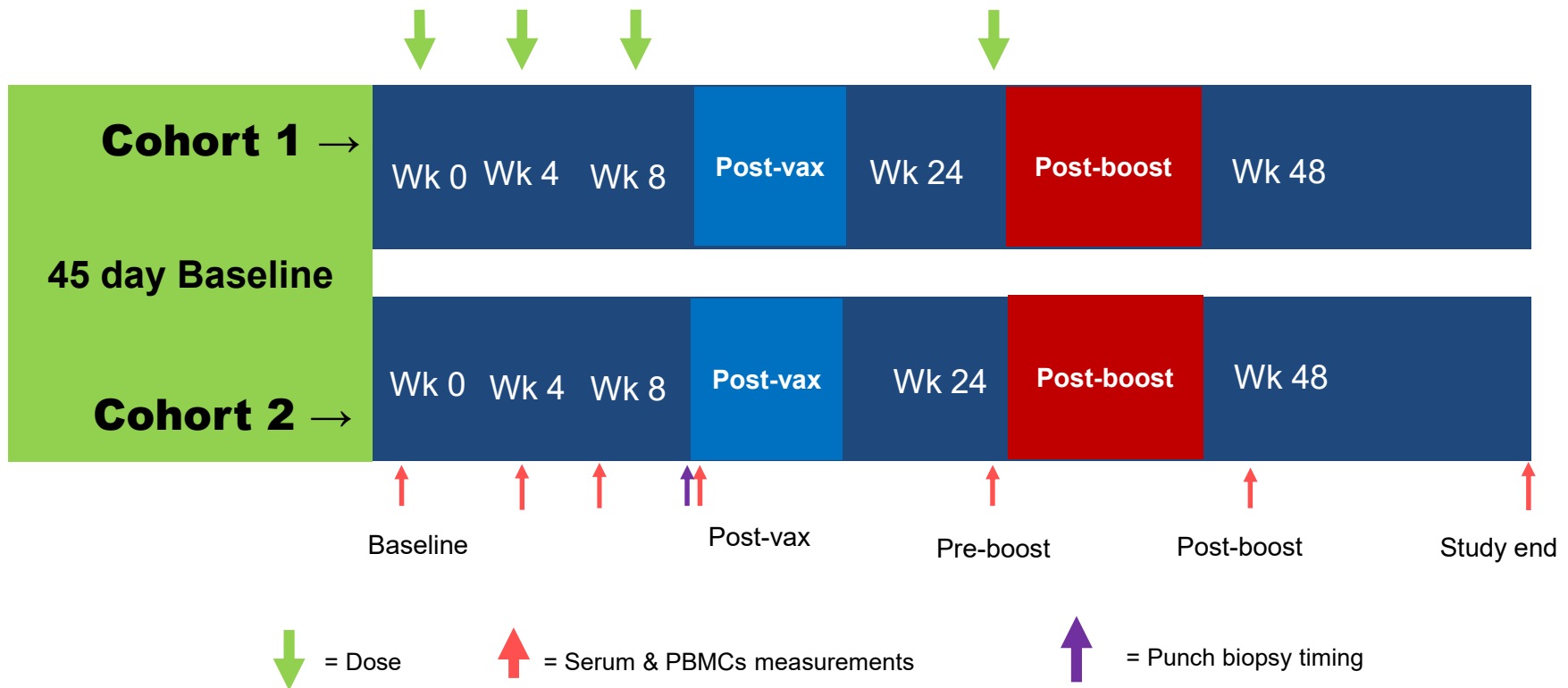
Total 44 HSV-2 positive patients enrolled

- Ratio 3:1 vaccine to placebo\ vaccine dose 0.5mg per injection
- Two injections of 500mcg (1.0mg total) per vaccination
- Three vaccinations plus a booster after 6 months

Two study cohorts:

- Cohort one: one injection in each (left and right) forearm per dose
- Cohort two: both injections into the left forearm within close proximity
- Samples from daily swabbing, blood samples and skin biopsies

HSV-2 Phase IIa study design



HSV-2 Phase IIa study endpoints



Primary endpoint:

To evaluate the safety and tolerability of two injection regimens of the HSV-2 DNA vaccine (COR-1) compared with placebo, administered by intradermal (ID) injection as three, 4-weekly doses followed by a 6-month booster to otherwise healthy, symptomatic Herpes Simplex Virus type 2 (HSV-2) positive subjects

Secondary endpoint:

To investigate the impact of COR-1 on the induction of an antigen specific humoral and/or cell mediated immune response against envelope glycoprotein D of HSV serotype 2 (gD2)

Exploratory endpoints:

- To evaluate the effect of COR-1 on HSV-2 shedding
- The incidence of symptomatic HSV-2 genital recurrence; and
- The nature of immunological responses to COR-1, including local tissue responses



HSV-2 Phase IIa results

Safety data summary



- Total of 44 patients enrolled
- Study primary endpoint met with no safety issues
- Dosed with 1.0mg of vaccine or placebo (ratio 3:1)
- Vaccine = COR-1 (n=34)
- Placebo = buffer solution used to formulate vaccine (n=10)
- 8 withdrawals
- None due to vaccine
- No serious adverse event (SAE) reported due to vaccine
- One moderate adverse event (AE) reported related to vaccine
- All AEs related to, probably or possibly related to vaccine were mild

Lesion outbreaks



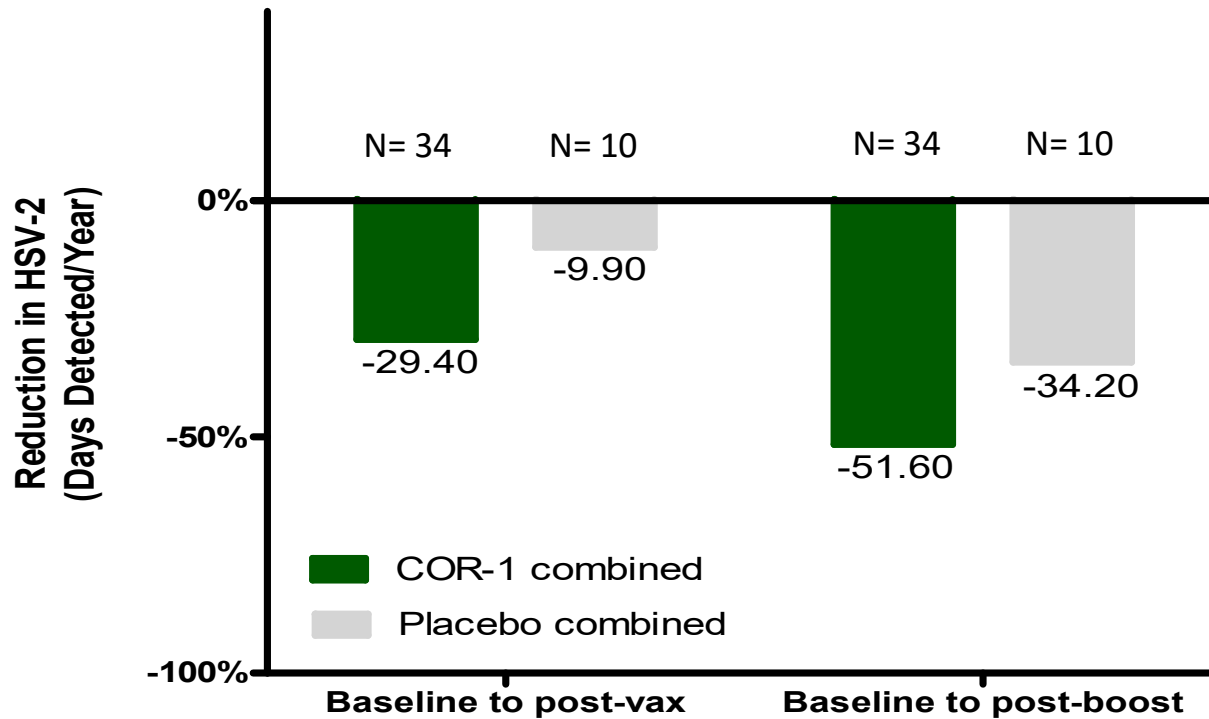
- Lesion outbreaks measured based on self-reported observations (therefore a subjective measure)

Confirmed by clinical trial site investigator and through lab testing

- Incidence of lesion outbreaks similar in vaccine and placebo groups
- Percentage of subjects with no outbreaks post vaccination in the vaccine group (29.4% n= 10) compared to the placebo group (10.0% n=1)
- No viral load differences observed between vaccine and placebo subjects at any time during the study

Viral shedding data

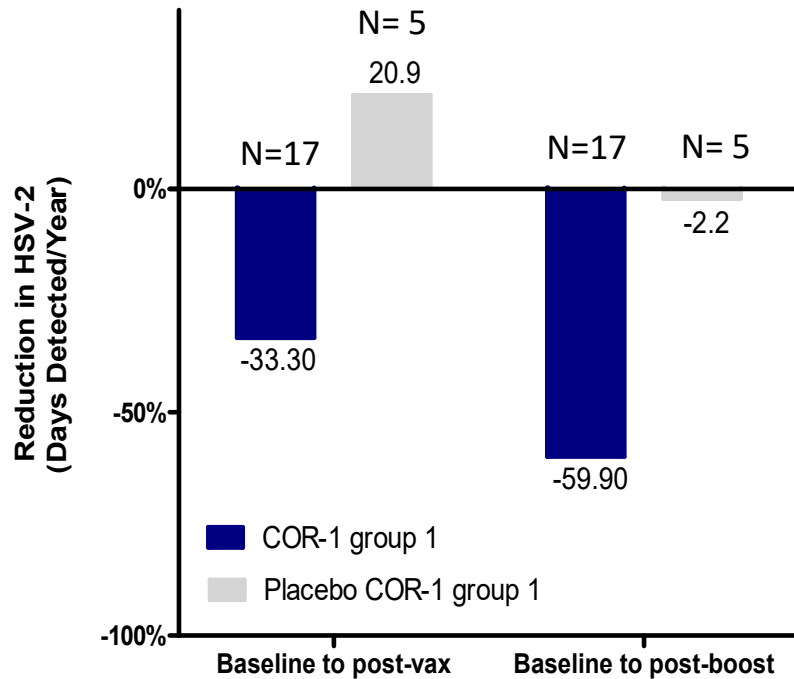
Combined cohort 1 & 2 and combined placebo viral shedding data



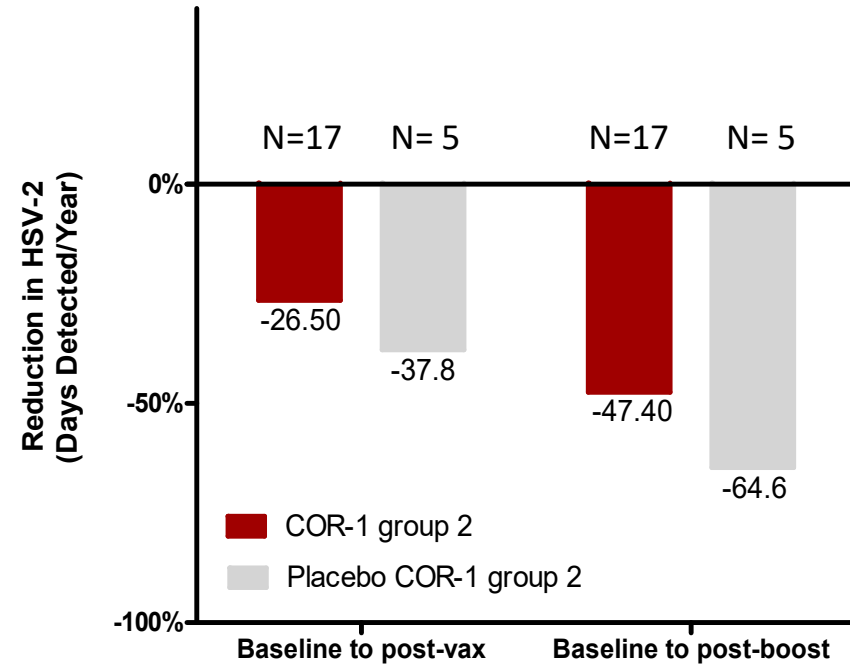
Viral shedding data



Cohort 1



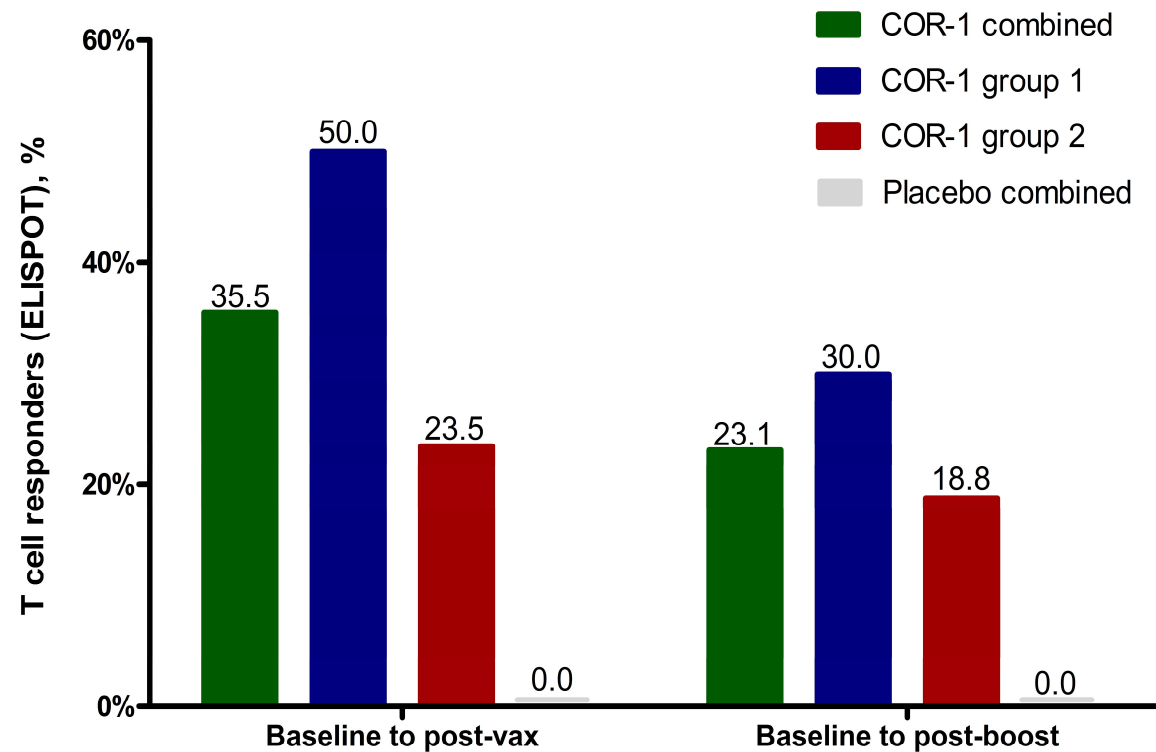
Cohort 2



T-cell response data

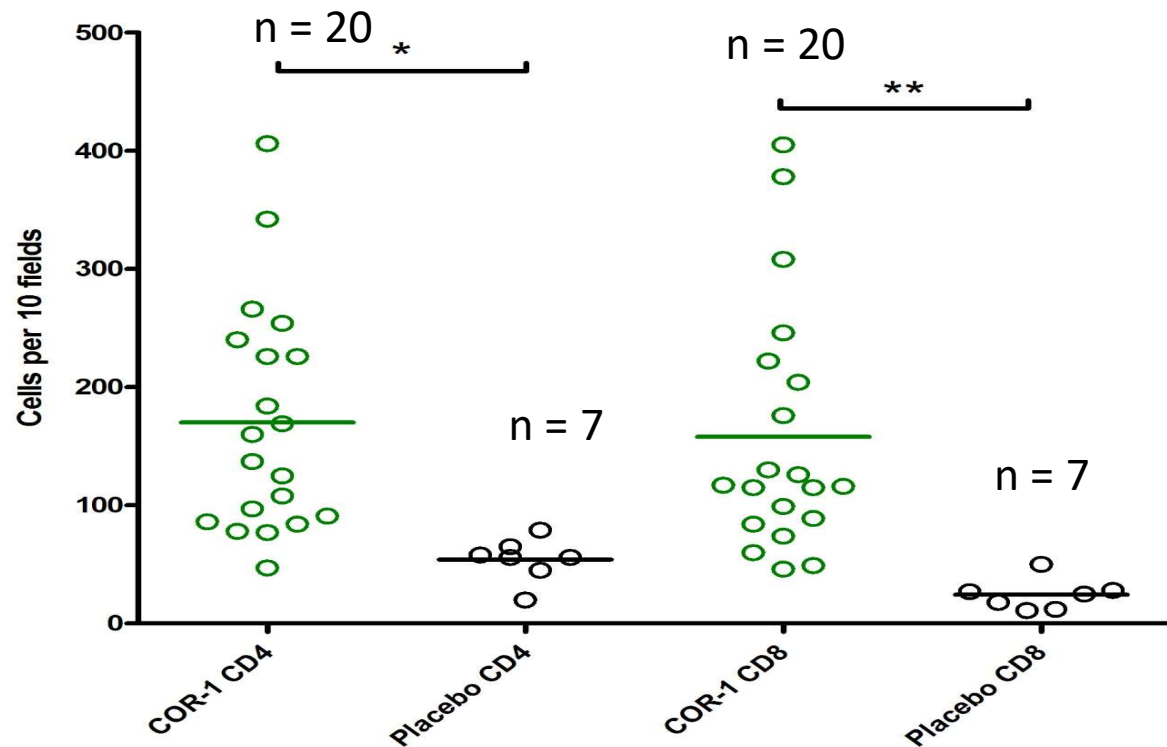
Conclusion:

- Strongest T-cell response in 50% of cohort 1 patients
- Highest post initial vaccination
- No T-cell response seen in placebo groups
- Vaccine therefore having T-cell activation response



Injection site tissue analysis

- Voluntary punch biopsy taken 48 hours after third dose of COR-1 or placebo and cell surface markers analysed by Immunohistochemistry
- Biopsy measuring local tissue for CD4 and CD8 cells
- Significant difference in number of CD4 and CD8 cells for vaccine subjects compared to the same cell types in placebo subjects



* p < 0.05, unpaired t-test, 2-tailed

Time to recurrence



| | Median time to first recurrence |
|---------|---------------------------------|
| Vaccine | 6.6 months |
| Placebo | 1.2 months |

- Recurrence is the time before another HSV-2 related outbreak and related symptoms
- Vaccine groups had much longer time to recurrence compared to placebo

Phase IIa data summary



- Study primary endpoint met - no safety issues with the vaccine
- Results indicated that the vaccine strongly stimulated cellular activity
- Supported by injection site biopsy data showing elevated CD4 & CD8 cells in skin tissue
- Viral shedding data shows greater reduction in viral shedding data in vaccine study subjects compared to placebo group
- No significant difference between placebo and vaccine groups for viral outbreaks
- Longer time to recurrence in vaccine group compared to placebo group

HSV-2 path forward



Next step in seeking to improve efficacy by:

- Trialing higher doses in a Phase IIb
- Analysing other intradermal delivery methods
- Continuing to explore complementary approaches to improve immune response

Immuno-oncology

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Cancer Immunotherapy

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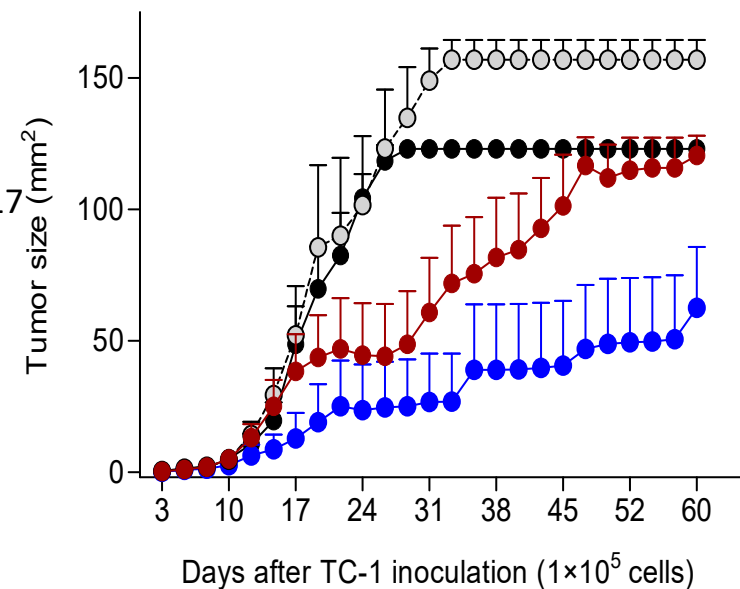


- Core RNA & DNA technology platform for multiple IO targets
- Initial programs against HPV related cancers
- Targeting E6 & E7 antigens

Multiple approaches:

- RNA immuno-oncology collaboration progressing well
- HPV Head & Neck cancer Phase Ib study due to start in 2017
- In combination with checkpoint inhibitor
- Also therapeutic for cervical cancer ready for Phase Ib
- Recent publication showing synergy with HPV vaccine and checkpoint inhibitors
- *J of Immunotherapy Vol. 40, No. Feb/Mar 2017 pg 62-69*

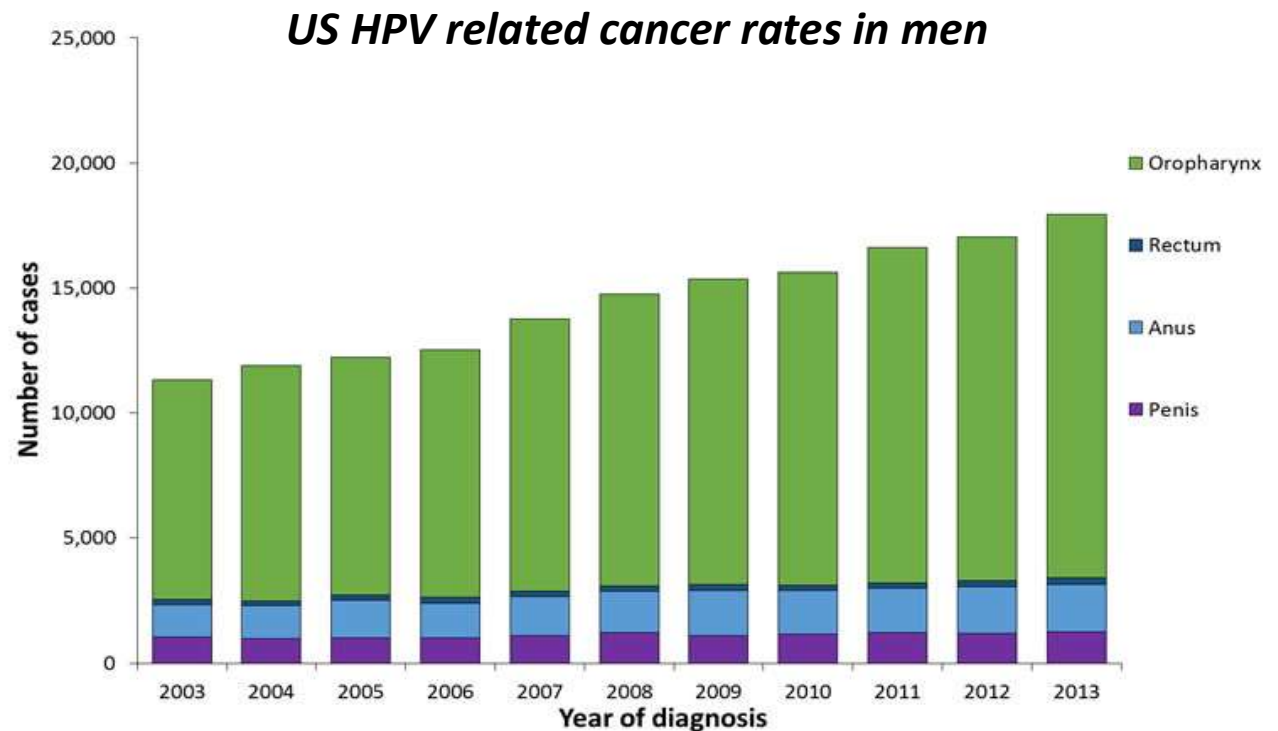
- Unimmunized
- Unimmunized + α -PD-L1
- HPV DNA vaccine
- HPV DNA vaccine + α -PD-L1



Initial focus HPV related cancer



- Rates of HPV related cancer increasing
- In the US the rates of HPV related cancer is increasing (10.8 per 100k to 11.7 per 100k 2008-2012)
- Admedus multiple programs targeting HPV related cancers



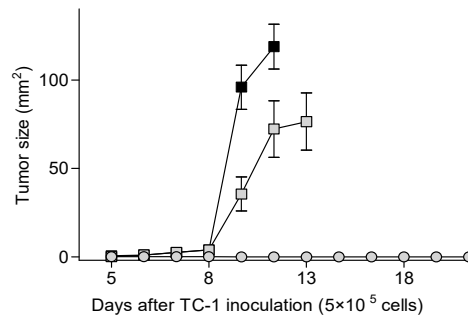
Reproduced from the CDC website

Immuno-oncology preclinical data

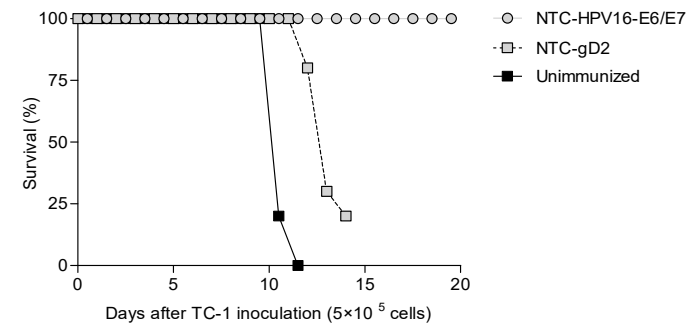


- Pre-clinical data in the TC-1 HPV translated mouse model
- DNA vaccine given 3 & 7 days post with clear benefit in survival rates and tumour size reduction

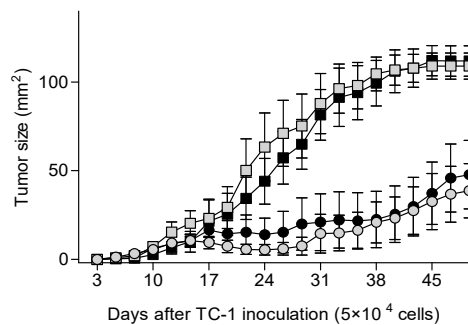
A Prophylactic immunization



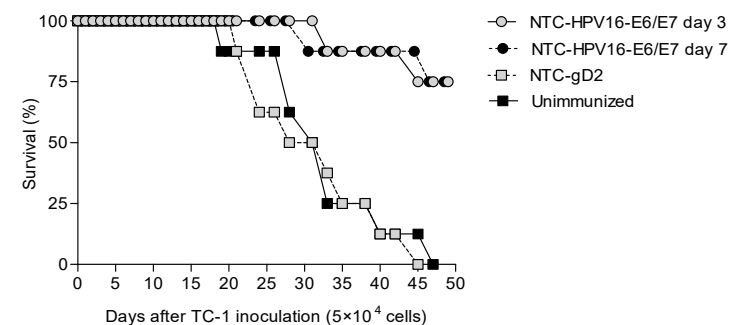
B



C Therapeutic immunization



D



Head & Neck Phase I study



- Initiating the study as soon as possible
- Work in conjunction with oncologist in Brisbane
- Two part study
- Part one – HPV safety in remission HPV head & neck patients
- Part two – safety in later stage HPV head & neck patients
- Primary endpoint of safety and secondary markers around immune response
- Clinical trial of vaccine in combination with a PDL-1 inhibitor based on strong pre-clinical data

RNA Program

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RNA therapeutic vaccine program



- Platform for RNA therapeutic targeting antibody & T-cell activated responses
- Can be applied to multiple RNA delivery technologies
- Initial program targeting HPV in collaboration with RaNA Therapeutics
- Program using a combination of the two Company's technologies
- Using lipid nanoparticle encapsulation technology
- Initial data has shown clear antibody and T-cell responses
- Initial animal studies in 2017 in TC-1 HPV cancer model

Company summary



- Results from HSV-2 Phase IIa shows initial T-cell responses
- Next steps to further develop the HSV-2 vaccine and improve patient responses
- Have initiated the HPV head and neck Phase Ib study
- Have ongoing RNA collaboration with RaNA targeting HPV



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Company milestones



- Initiating Head & Neck Phase I clinical study
- First patient dosed in Head & Neck study
- Final Head & neck data
- Initial RNA animal data
- Improved HSV-2 delivery



Next Steps



- Review all external funding options
- Prioritize the multiple portfolio opportunities
- Review structural options
- Continue developing program plans
- Streamline development timelines / resource model





Wayne Paterson
CEO
Admedus Ltd (ASX:AHZ)

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