Disclaimer This presentation includes forward-looking statements regarding Bionor Pharma ASA, including projections and expectations, which involve risk and uncertainty. Such statements are included without any guarantees to their future realization. Although Bionor Pharma ASA believes that the expectations regarding the Company reflected in such forward-looking statements are based on reasonable assumptions, no assurance can be given that such projections will be fulfilled. Any such forward-looking statement must be considered along with knowledge that actual events or results may vary materially from such predictions due to, among other things, political, economic, financial or legal changes in the markets in which Bionor Pharma ASA does business, and competitive developments or risks inherent to the Company's business plans. Many of these factors are beyond Bionor Pharma ASA's ability to control or predict. Given these uncertainties, readers are cautioned not to place undue reliance on any forward-looking statements. The Company does not intend, and does not assume any obligation, to update the forward-looking statements included in this presentation as of any date subsequent to the date hereof.

Content

Brief update on Bionor Pharma
Steen Krøyer, CEO

Status and further development of the HIV vaccine research
Dr. Jerome "Jerry" Zeldis and Prof. Angus "Gus" Dalgleish

Business development
Gregg Lapointe, US Business Development Excecutive

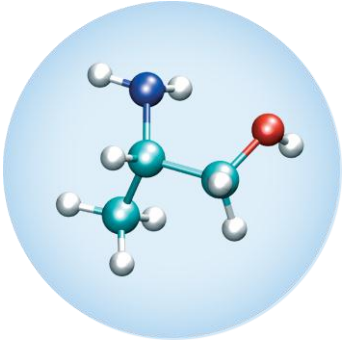
November 2012

BIONORPHARMA

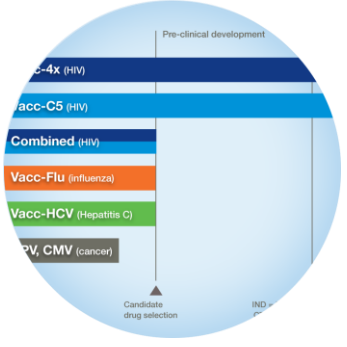
The company

Who we are

Norwegian led



Proprietary platform



Attractive portfolio

Experienced management

World class advisors

Substantial investment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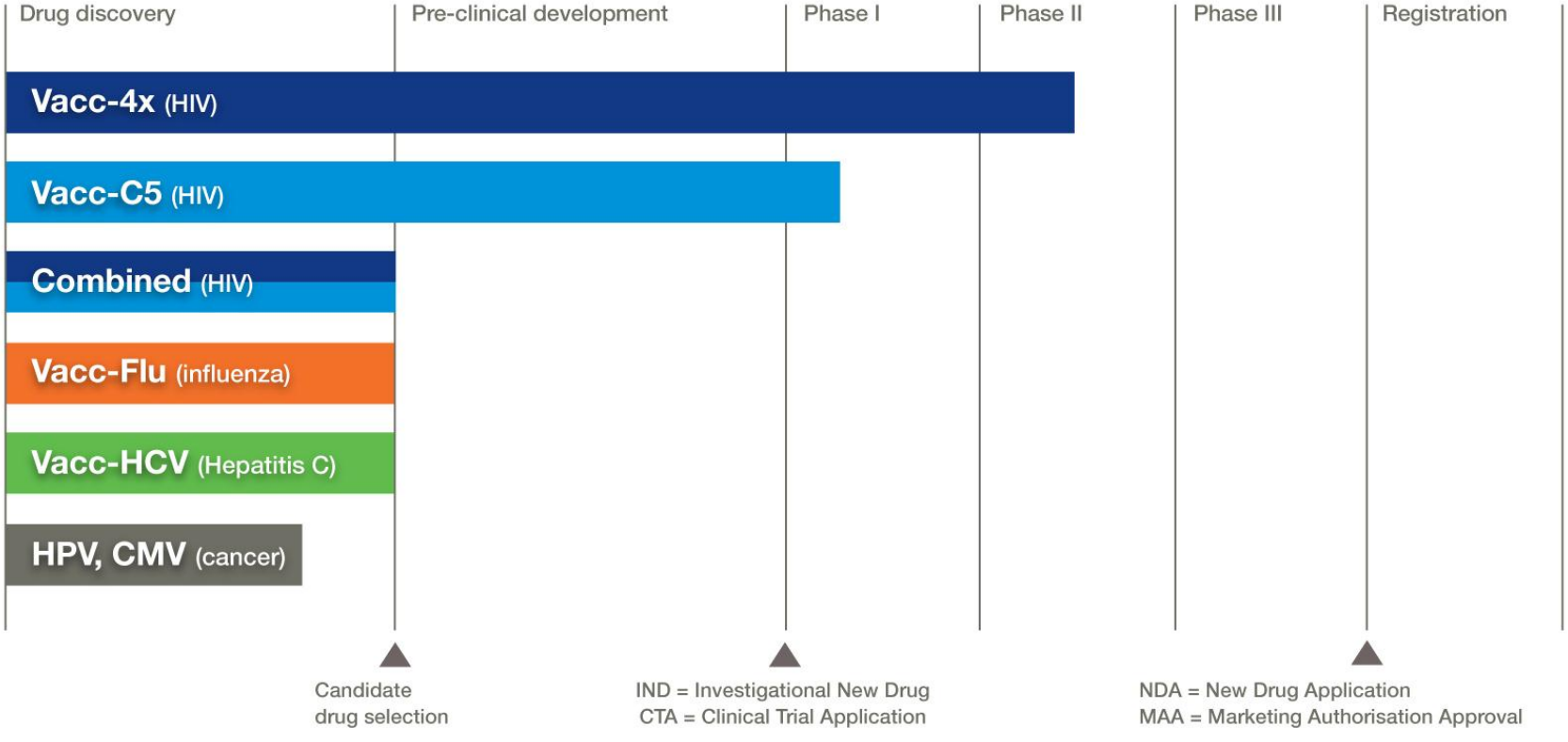
Search...
Bionor Pharma is a leading vaccine company, searching for breakthrough treatments for HIV and other deadly viruses.
Modified Peptide based vaccines
There are many benefits of using modified peptides, and among the most important are the safety profile, and that they are effective to administer for people at all ages, all over the world.
1
2
3
Read more »
Latest news
Hide mandatory notifications of trade
Bionor Pharma presents data from HIV vaccine research at scientific meeting in Baltimore
SCIENTIFIC 14.10.2012
Baltimore 14.10.2012 - Research on Vacc-4x and Vacc-C5 is today presented at the Annual Meeting of Institute of Human Virology
Bionor Pharma featured in Positiv magazine
MEDIA COVERAGE 28.09.2012
Featured content
Clinical Advisory Board
Our Clinical Advisory Board consists of prominent experts within the fields of vaccines and immunology. Meet
VACC-C5
Aim to cure HIV infection
Whereas Vacc-4x appears to kill virus-producing cells, Vacc-C5 has the potential to reduce the damaging
MacBook Pro

Bionor Pharma Pipeline



Ongoing studies

Three studies at sixteen sites

Vacc-4x reboost

Reboost with Vacc-4x in patients from the phase II study

Approval expected: USA + 4 European countries, Q4 2012 , approx.11 clinics, ca. 40 patients

First patient enrolling: End of Q4 2012

Design: Two immunizations of Vacc-4x while on ART, then up to 16 weeks of treatment interruption. Total study period 37 weeks.

Funded: Globvac (Norwegian Research Council) and Bionor Pharma ASA

Patient group: Participants from the previous phase II study with Vacc-4x

The primary endpoints: Changes in viral load compared to the previous study and immune responses to the vaccine

Aim of the study: To determine whether a lower viral load level (“set point”) can be achieved by re-boosting previously vaccinated HIV infected patients

Vacc-4x + Revlimid®

Vacc-4x in combination with Celgene`s immune modulator Revlimid®

Approved: Germany, August 2012, 4 clinics, approx. 36 patients (~12+24)

First dose group initiated treatment: October 2012

Design: First dosing-study with ~12 patients, determining “maximum tolerated” dose of Revlimid®. Then 24 patients for 26 weeks.

Funded: Jointly with Celgene, owner of the blockbuster cancer drug and immune modulator Revlimid®

Patient group: Well controlled viral load on conventional HIV medicine (ART), but failing to regain normal immune function (15-20% of all HIV patients)

Primary endpoints: Changes in the amount of CD4 T-cells and immune responses to the vaccine

Aim of the study: Determining whether the combination of Vacc-4x and Revlimid can result in improved response to Vacc-4x in HIV infected patients with poor immune recovery (low CD4 T-cells despite well controlled viral load on ART)

Vacc-C5

Clinical phase I/II study

Approved: Oslo University Hospital, May 2012, 36 patients

First patients treated: November 2012

Design: “First time in man” open study, three different dose levels of Vacc-C5, each with two different adjuvants (supporting agents). Twenty six weeks study period for each patient.

Funded: Bionor Pharma ASA

Patient group: Well controlled on conventional HIV medicine

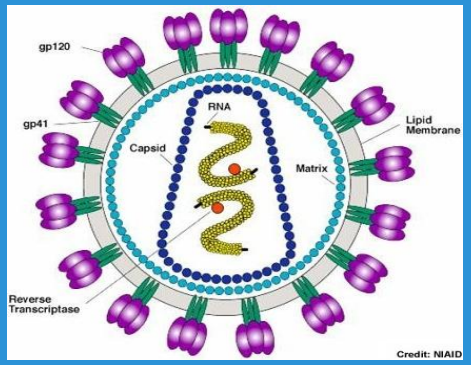
Primary endpoint: Evaluation of the vaccine’s safety

Secondary endpoint: Antibody responses to the vaccine.

Aim of the study: To determine whether antibodies to two specific , conserved areas of the HIV virus (C5 and gp41) are induced in HIV patients

Bionor Pharma – The pathogenesis of HIV and its implications for vaccines

Angus Dalgleish, FMedSci / Jerome B. Zeldis, MD



BIONORPHARMA

Angus "Gus" Dalgleish

MD FRCP, FRACP, FRCPath, FMedSci

Professor, St. George`s, University of London

Professor of Oncology at St. George's University of London since 1991.

He has been involved with HIV research since the first descriptions of AIDS. Working as a clinical fellow with Robin Weiss he described the use of CD4 as the main receptor for HIV and was the first to associate HIV with the outbreak of SLIM disease in Uganda.

His main interest is the pathogenesis of HIV that has to induce immune activation before the infection can proceed to clinical AIDS. His group was the first to suggest that the C5 region of gp120 could act as if it were a foreign transplant antigen (alloepitope) and induce the activation that precedes AIDS and also to suggest it as a potential therapeutic target.

Professor Dalgleish has also pioneered the use of cancer vaccines and is principal of the Cancer Vaccine Institute and has been principal and clinical investigator on numerous vaccine trials. He has published over 300 peer reviewed papers and co-edited five books including HIV and the New Viruses and Tumor Immunology, as well as numerous book chapters.

Jerome B. Zeldis, MD

CEO of Celgene Global Health and Chief Medical Officer of Celgene Corporation, Summit, NJ.

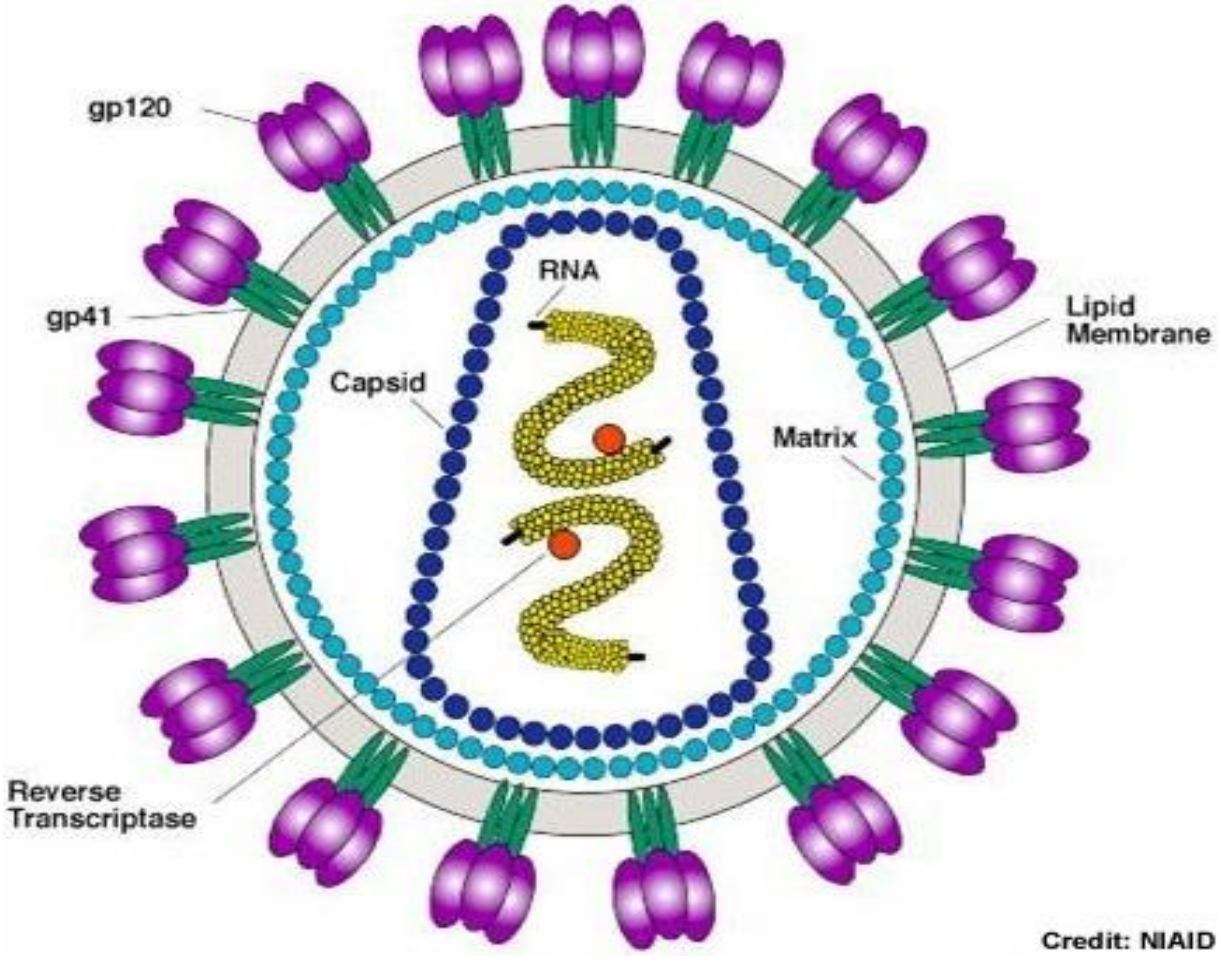
Prior to that he was Celgene's Senior Vice President of Clinical Research and Medical Affairs. He attended Brown University for an A.B., M.S., followed by Yale University for an M.Phil., M.D., Ph.D. in Molecular Biophysics and Biochemistry (immunochemistry). Dr.

Zeldis trained in Internal Medicine at the UCLA Center for the Health Sciences and Gastroenterology at the Massachusetts General Hospital and Harvard Medical School. He was Assistant Professor of Medicine at the Harvard Medical School, Associate Professor of Medicine at University of California, Davis, Clinical Associate Professor of Medicine at Cornell Medical School and Professor of Clinical Medicine at the Robert Wood Johnson

Medical School in New Brunswick, New Jersey. Prior to working at Celgene, Dr. Zeldis worked at Sandoz Research Institute and Janssen Research Institute in both clinical research and medical development. He has been a board member of a few start-up biotechnology companies and is currently on the board of the Semorex Corporation, NJ chapter of the Arthritis Foundation and the Castleman's Disease Organization. He has published 112 peer reviewed articles and 24 reviews, book chapters, and editorials

Summary

- HIV causes AIDS probably by chronic immune activation
- We propose that chronic inflammation:
  - Is induced by HLA-transplant antigens, like regions encoded in HIV-1 gp120/gp41
  - Especially the C5 and C2 parts of gp120
- Antibodies to C5 region - associated with non-progression
- CTL responses to gag, Vacc4x, can reduce viral load
- Vaccination to C5 region and gag may prevent AIDS
- IMiDs such as lenalidomide may enhance vaccines


gp120
gp41
RNA
Capsid
Matrix
Lipid
Membrane
Reverse
Transcriptase
Credit: NIAID

Current Failed HIV vaccines

- Based on dominant neutralising sites on gp120 V3 loop
- Large scale prophylactic vaccine trials to V3 loop (Vaxgen and Merck/Wyeth) failed to protect

  Vaccines developed a higher viral burden compared to controls
- V3 loop is most dominant and variable region

  Probably deflects immune responses to other essential epitopes
- Other epitopes that are non-neutralising

  Largely ignored by HIV community

Immune activation is always required for AIDS to develop

- Why do some people not get AIDS
- Why do chimpanzees not get AIDS
- The only difference is that there is no evidence of immune activation, It is chronic and associated with inflammation and has auto immune features.
- How does HIV cause Immune activation
- Can we switch it off
- This is the unique approach included by Bionorpharma
- Chronic immune activation is like background noise on the radio which prevents the signal from being heard!

Lessons from SIV Models

Monkey Species	Viral Load	Activation	Outcome
 Rhesus macaque	High ⇧⇧	High ⇧⇧	Disease Progression & AIDS.
 African green (Agm):	Low ⇩⇩	Low ⇩⇩	Non Progression No Pathogenesis
 Sooty mangabey	High ⇧⇧	Low ⇩⇩	Non Progression No Pathogenesis

How does HIV provoke chronic immune activation in the majority of humans?

Hypotheses by which HIV Causes Immune Activation

1. Hypervariability of HIV antigens **Not likely**

2. Superantigens **Not likely**

3. Allostimulation (GVHD) **Possible**

Graft Versus Host Disease (GVHD)

- Chronic GVHD is very similar to AIDS
  - Occurs when the body tries to reject a transplant kidney/liver etc.
  - When drugs are used to suppress this the transplant(graft) induces T cells to attack the host.

- Similarities

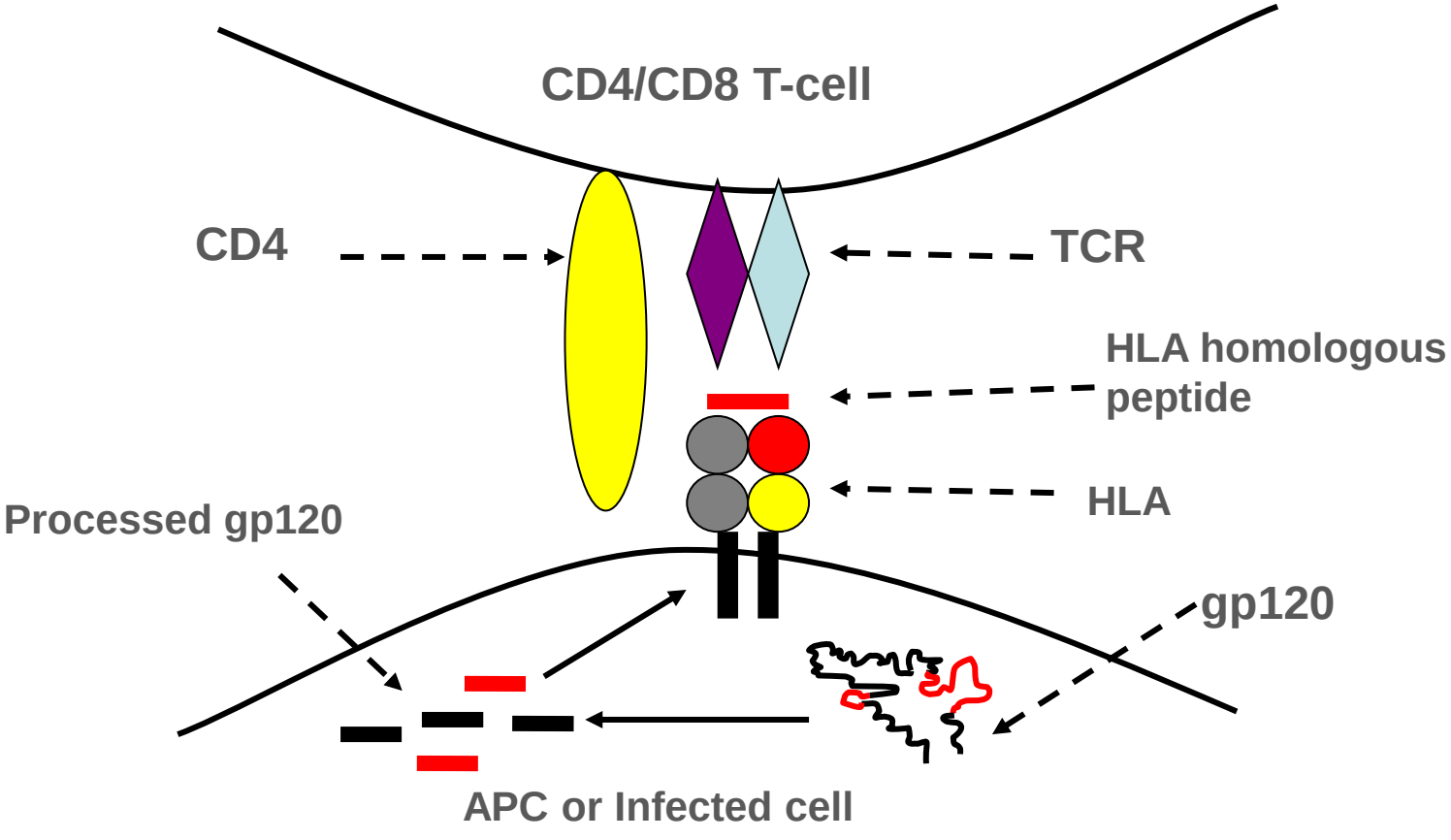
  (Clinically so similar you would need an HIV test to tell the difference)
  - Opportunistic infections, weight loss, lymphadenopathy, lymphomas, skin lesions
  - Pan immune activation with CD4 suppression

Shearer (NEJM 1983)

Ways ‘HIV’ causes allogeneic responses similar to GVHD?

- Structural mimicry between transplant antigens and the virus
- Peptide sequence similarities causing antigen presenting confusion

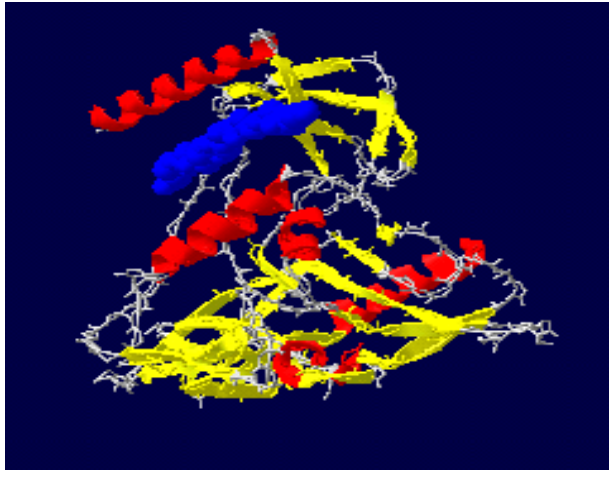
Indirect HLA Mimicry induced immune activation



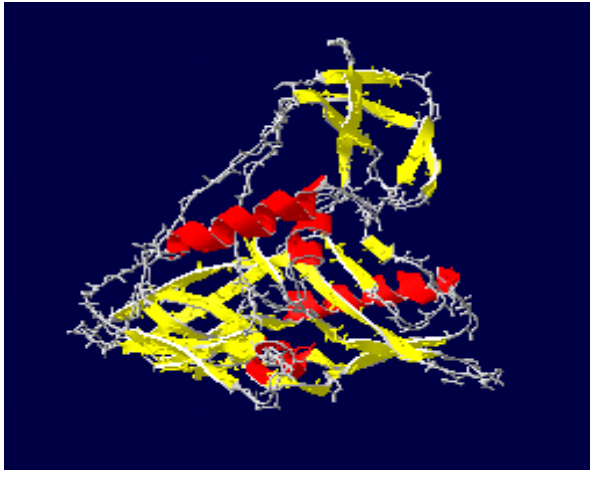
Crystal structure and modelling

HLA DR1 + peptide

GP120 + peptide



GP-120 ΔC5-mutant



Predictions from molecular model

- HLA-B8 would be fast progressors
- HLA-B27 slow progressors (Gore MRC, 1989)
- Chimpanzees would have restricted HLA

Bontrop later determined they are all HLA-B57(27)

HIV-1 gp120 C5 region and direct HLA structural mimicry

- Modelling predicts alpha-helix similar to HLA class I and II antigen binding sites

Hounsell et al 1991,Mol Aspects of Med

- Anti-C5 antibodies cross-react with HLA class I peptide binding domains

Grassi et al, 1991,J exp med

- C5 domain alpha-helix crucial for peptide binding

Cadogan et al, 2008, AIDS Res Hum Retro

Non-neutralizing Anti-C5 is associated with non-progression

- 70% of seronegative partners of AIDS patients have antibodies to HLA and/or C5 of gp120

  Brown et al. AIDS 2000

- Anti-C5 region antibodies associated with slow progression

  Loomis-Price et al, J Infect Dis. 1998
  Lifson AR et al, J Infect Dis 1991
  Warren RQ et al, J Clin Immunol 1991

- Loss of anti-C5 response associated with progression.

  Wong MT et at, JID, 1993

Walter Reed Cohort: Humoral anti-C5 responses

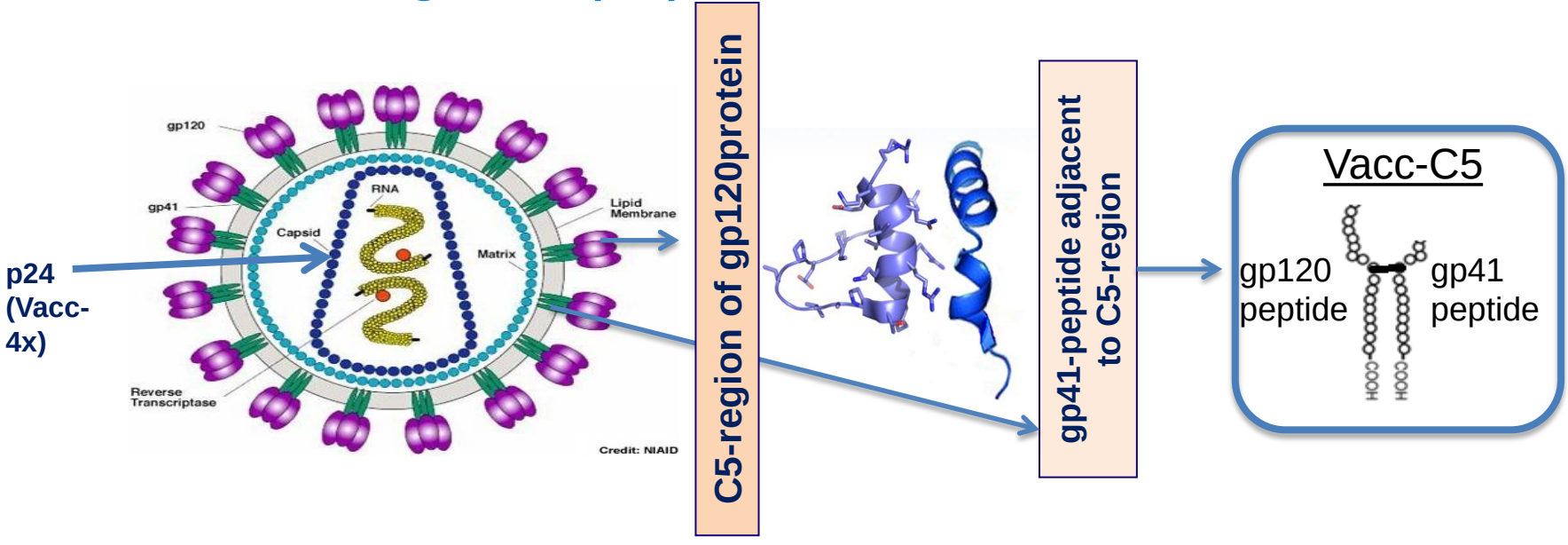
Table 2. Reactivity of specific peptides with sera from Walter Reed progression cohort.

Purpose, peptide	Sequence	Median reactivity[a]	
		Rapid progressors	Slow progressors
Distinguish rapid from slow progressors			
101	VEQMHEDIISLW	**2.7**	<0
301	TRKSIRIQRGPG	**36.8**	6.9
341	KQIASKLREQFG	0.6	**2.3**
353	NNKTIIFKQSSG	**5.1**	1.7
413	TLPCRIKQFINM	<0	**2.8**
497	TKAKRRVVQREK	19.4	**99.0**
501	RRVVQREKRAVG	3.5	**50.4**
581	VERYLKDQQLLG	0.1	**19.1**
597	SGKLICTTAVPW	104.0	**173.0**
653	KNEQELLELDKW	1.4	5.6
657	ELLELDKWASLW	11.6	31.2

What does this mean?

- Antibodies to C5 prevent immune activation and hence prevent disease progression
- If we induce these they could neutralize the disease
- Stopping activation will stop virus production

Vacc-C5 – targeted peptides

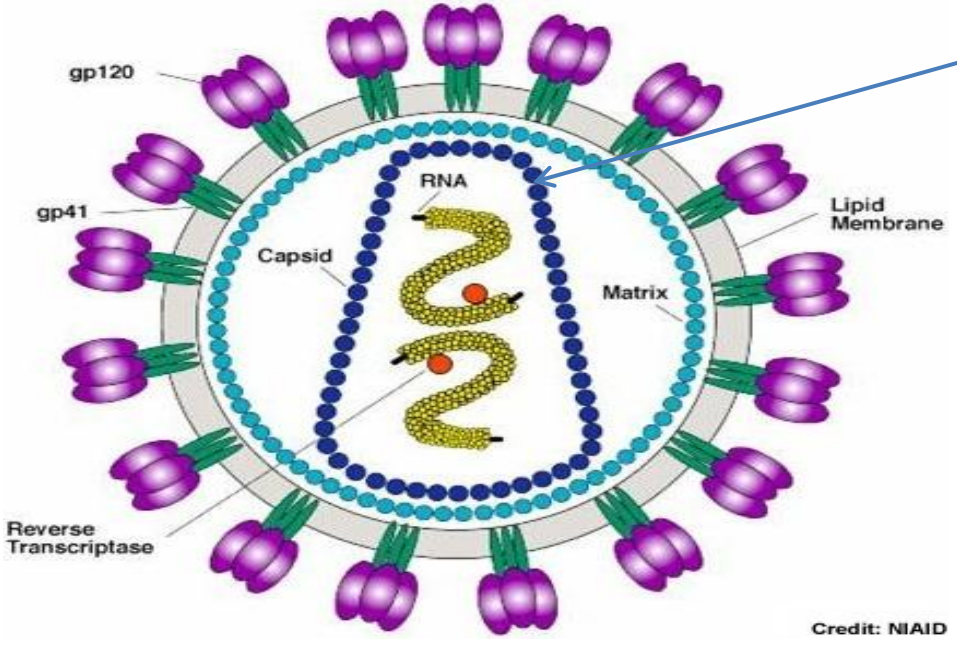


- Vacc-C5 developed on basis of modified synthetic peptides from the C5 domain and gp41
- Vacc-C5 targets B-cells for production of antibodies
- We predict that anti-C5 antibodies will block immune activation

Turning off activation

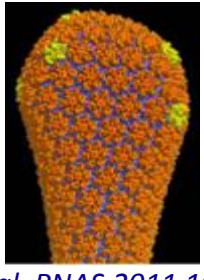
- This will allow other signals to be heard
- Vacc-4x which already inhibit viral loads will be rendered even more effective
- Activation is like background noise on the radio, upon tuning, the noise goes and you can hear the signal

Vacc-4x: Targeting the p24 Capsid



p24 (Vacc-4x)

- Consists of 4 modified **peptides** corresponding to conserved domains of HIV-1 $p24^{CA}$
- Sustained immune responses to $p24^{CA}$ are associated with delayed disease progression*
- Strong responses to Gag are associated with virus control (LTNP) in the absence of ART¤



Dahirel V et al. PNAS 2011 108:11530-11535

* *Weber et al. 1987 Lancet 1:119-22 ; Cheingsov-Popov et al. 1991 BMJ 302 :23-6*
¤ *Kiepela et al. 2007 Nature Med. 13:46-53; Zuniga et al. 2006 J. Virol 80:3122-5.*

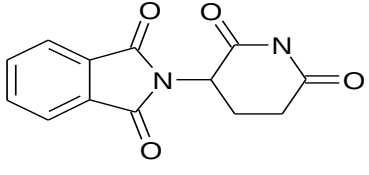
Vacc-4x – Completed clinical studies

- **1999-2000**
  - Open study, 11 patients. 100% immune response. Safe vaccine without side effects
- **2003-2004 Phase II**
  - Open study, 40 patients (CD4 count at inclusion >300 cells/μl), ART-free period on average 31 months
- **2010 Phase II-reboost**
  - Open study, 7 years after initial phase II. 26 patients from the Phase II, with 2/3 of patients showing active memory response. Immune response enhanced after re-vaccination (reboost)
- **2008-2010 Phase II**
  - Placebo-controlled multicenter study. 18 centers in USA and Europe, 135 patients (CD4 count at inclusion >400 cells/μl). Statistically significant reduction of HIV VL in active group compared to placebo
  - Supportive immunological data

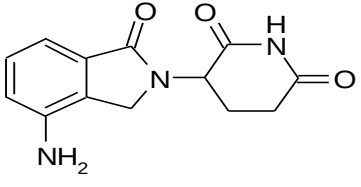
IMiDs® As Adjuvants

- Drugs derived from thalidomide
  - Selected on properties to inhibit TNF production
  - Qualitatively and quantitative different from each other

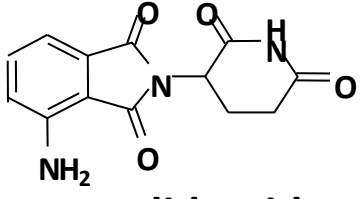
- IMiDs® adjuvant-like properties
  - Expand and enhance NK cell function
  - Enhance ADCC and antigen presentation by APCs
  - Co-stimulate T cells : CD8 > CD4
  - Enhance IL-10 and IL-12 production
  - Modulate TNF expression



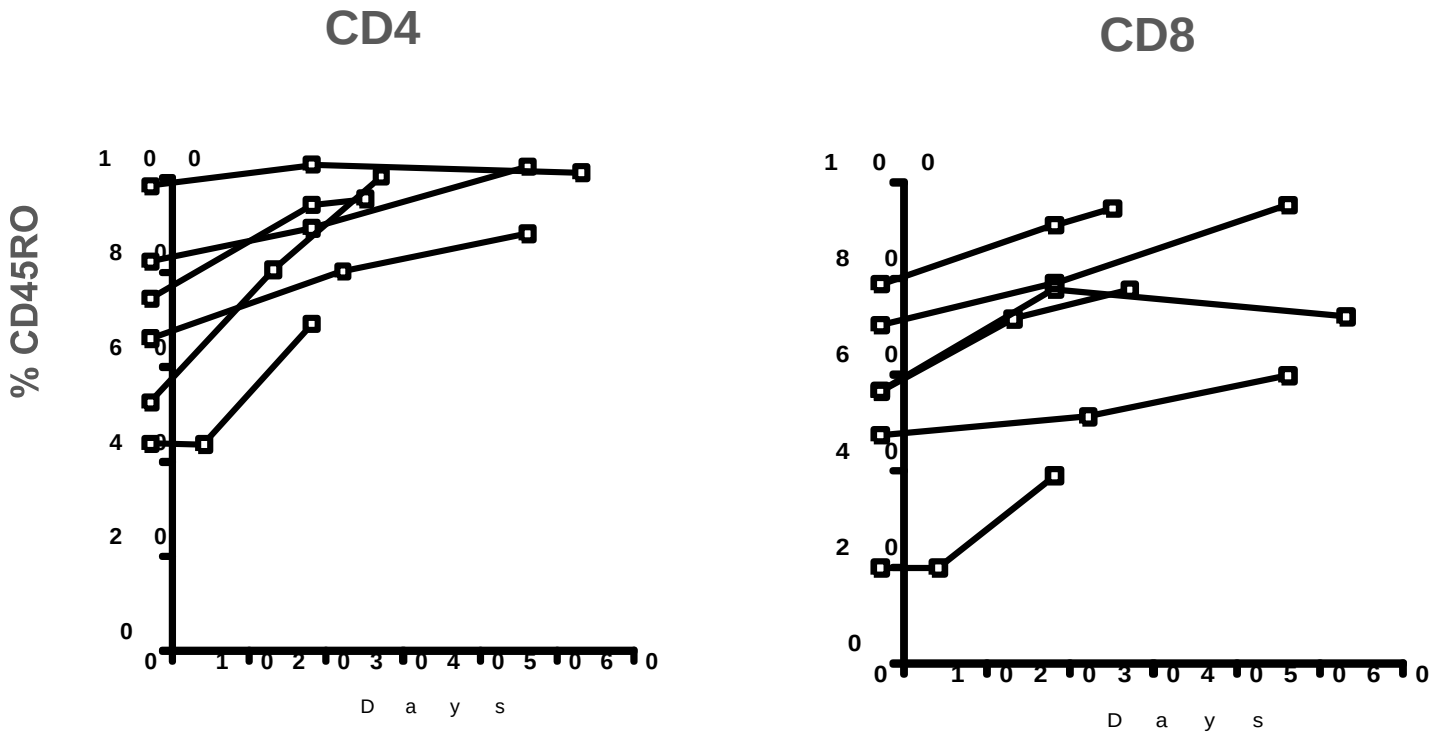
thalidomide



lenalidomide



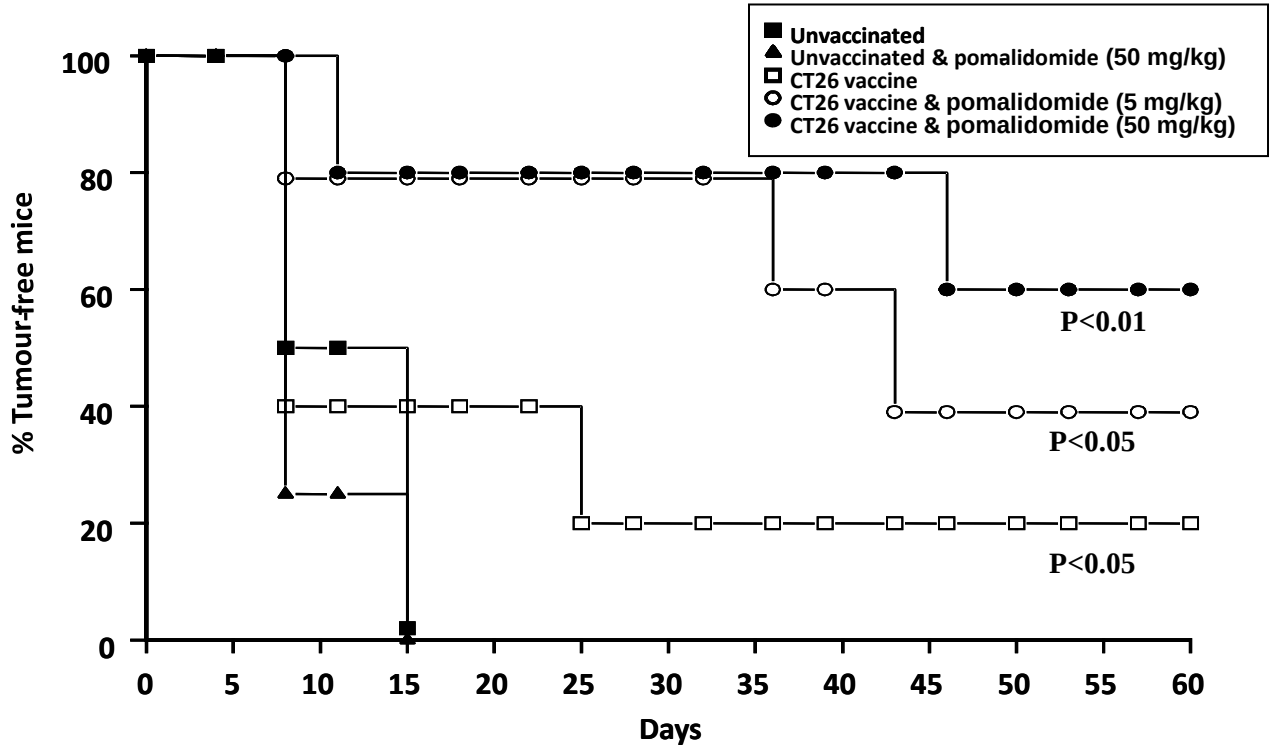
pomalidomide



- **CC-5013 treatment of melanoma patients with leads to increased % of**
  - **CD4+ and CD8+ T cells with no change in CD4/CD8 ratio**
  - **CD45RO+ T cells**
  - **Indicative of naïve cell (CD45RA+) activation**

Bartlett et al. Br J Cancer 2014, 90, 955.

Pomalidomide enhances the efficacy of a colorectal whole tumor cell vaccine

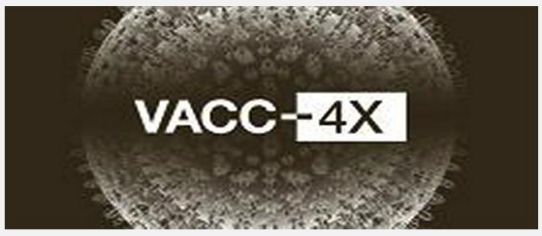


- Pomalidomide enhances survival of vaccinated mice
- Elicits long term protection from live tumor rechallenge
- No protection afforded in nude mice (T cells required)

Dredge et al. J Immunol 2002, 168, 4914.

Conclusions

- Therapeutic non-neutralising vaccines
  - May prevent progression to AIDS
  - Might also prevent HIV infection
  - Might enhance other Ag specific vaccines (e.g. Vacc4x)
- Oral IMiDs® should enhance both vaccines
  - By a number of physiological mechanisms
- This approach might apply to other chronic infections
  - HCV
  - Malaria



HIV vaccine Vacc-4x

HIV vaccine Vacc-C5

Bionor Pharma – Business Development

Gregg Lapointe, Business Development Process

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Two Critical Steps

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Information Gathering & Preparation

Materials

- **TPP's** (For Key Assets)
- **Market & Commercial Research** (Navigant, BCG, McKinsey, KOL's + Community Dr, etc. Market entry/ramp up, pricing, commercialization options)
- **IP Position** (Patents, Processes, Regulatory exclusivity)
- **Clinical/Regulatory FDA Clarity** (Cost, Timelines, Inflection Points)
- **News Flow** (Clinical Data, Patent Announcements, Other Application)
- **Financial** Analysis (Value, rNPV's, MC Simulations, DCF's, POS's, Key Assumptions)

Deliverables

- **Non-Confidential Teaser**
- **Full Briefing Book**
- **Complete Data Room**

Partnering Process

Activities

- **Identification of likely partners** (Vaccine Specific BD, Venture Sponsors w/in Big Pharma, others)
- **Key Meetings** (Bio Asia, Bio USA, JP Morgan, Regional Conferences, Others)
- **Diligence** (Access to Briefing Book, Data room, Management Q&A)
- **Partnering Solutions** (Research Agreements, License, M&A, which assets)
- **Indications of Interest & High Level Deal Terms**

Outcome

- **2-3 Potential partners**
- **Auction process?**
- **Execute Deal**

Upcoming events

Next Steps / Process

1. Complete TPP, Market Research, rNPV
2. Finalize Teaser / Briefing Book(s) / Data Room
3. Pilot Test Due Diligence / Partnering “lite” Perform Market Interest Test
4. Commence Full Partnering Activities (Bio(s), face2face meetings, outreach, candidate selection, “auction process”)