Defence Therapeutics
Corporate Overview

Uniquely Positioned and Versatile Technology
Defence Therapeutics is a Canadian Biotech developing next generation biopharmaceutical innovations for various immuno-oncology (IO) and infectious diseases (ID) indications.

Platform
An Accumulator (Accum™) suitable to enhance the delivery of proteins, RNA and DNA

Growth opportunity
● Strong versatility of the Accum™ platform
● Attractive capital structure of only 36 million shares outstanding with strong based shareholders.
● Well-positioned to achieve data-driven value-inflection points in the next 6-12 months

Experienced Team
Extensive experience in pre-clinical/clinical, business development, CMC and Regulatory
Management and Scientific Team

Sebastien Plouffe, Co-Founder, President and CEO
Financial expert and entrepreneur with 25+ years experience with public companies, strong management skills

Joseph Meagher, CFO
CPA with more than 20 years of experience and has served as CFO for several publicly listed companies

Carrie Cesarone, Corporate Secretary
A public companies’ legal affairs and corporate expert with more than 30 years of experience

Dr. Moutih Rafei, VP R&D
Professor at Université de Montréal and world renowned expert in Immuno-oncology

Dr. Simon Beaudoin, CTSO
Co-inventor of Accum technology. Expert in Protein Biochemistry
Board Members and Advisors

**Sebastien Plouffe, Co-Founder, President and CEO**
Financial expert and entrepreneur with 25+ years experience with public companies, strong management skills

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**Michael Pfleiderer, Biopharma Excellence Strategic Advisor**
Expert pharmaceutical advisor with focus on Europe, USA and Japan regulatory affairs

**Dr. Raimar Löbenberg, Director, Scientific and Regulatory Affairs**
Founder and Director of the Drug Development and Innovation Centre (U of A)

**Dr. Sarkis Meterissian, Director**
World renowned oncologist, Director of the Breast Center of the MUHC and MUHC Head of the Tumor Site Group

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**Dr. Riam Shammaa, Regen Capital Strategic Advisor and Expert in Cell Therapy**
Expert in biotech and healthcare and advisor with business focus on USA

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Regen Capital Strategic Advisor and Expert in Cell Therapy
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Current Challenges: IO and ID

- Standard of care currently ineffective against disseminated cancers
- Targeted biopharmaceuticals struggle with molecular obstacles, limiting their potential to become a therapeutic standard for human diseases (i.e. cancer)
- No "real" anti-cancer vaccine available (The Dendreon vaccine remains questionable!!)
- Absence of effective vaccines against various deadly pathogens

Urgent need for an enabling and first-in-class versatile technology
Global Market for Immuno-Oncology

Market forecast to grow at CAGR of 14.3%

https://www.reasearchandmarkets.com/reports/5309486
# Pipeline in Development

<table>
<thead>
<tr>
<th>DC VACCINE</th>
<th>INDICATION</th>
<th>DISCOVERY</th>
<th>PRE-CLINICAL</th>
<th>PHASE I - 2022</th>
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<tbody>
<tr>
<td>AccuVAC-D001</td>
<td>Lymphoma</td>
<td></td>
<td>NON-GLP</td>
<td>Q1</td>
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<tr>
<td>AccuVAC-D002</td>
<td>Melanoma</td>
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<td>GLP</td>
<td>Q2</td>
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<tr>
<td>AccuVAC-D003</td>
<td>Breast</td>
<td></td>
<td></td>
<td>Q3</td>
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<tr>
<td>AccuVAC-D004</td>
<td>Colon</td>
<td></td>
<td></td>
<td>Q4</td>
</tr>
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</table>

ADCs

- AccuADC-001
  - Breast/Gastric

- AccuADC-002
  - Breast/Gastric

AccuTOX

- AccuTOX-001
  - Lymphoma

- AccuTOX-002
  - Breast

COVID Vaccine

- AccuVAC-PT001
  - COVID-19

- AccuVAC-IN003
  - COVID-19

HPV Vaccine

- AccuVAC-PT009
  - HPV
**Accum molecule**

- **Bile acid**
- **NLS**

**Proprietary platform technology** with proven enhanced intracellular delivery

**Promotes delivery** of target product without non-specific protein/antigen degradation or interference

- Various applications in:
  - ADCs
  - Cancer Vaccines
  - ID Vaccines
- Full ownership of assets and IP
INTRODUCING THE DC VACCINE PROGRAM:
Pre-clinical proof of concept

AccuVAC-D001\textsubscript{L} (Lymphoma)
AccuVAC-D002\textsubscript{M} (Melanoma)
AccuVAC-D003\textsubscript{B} (Breast cancer)
AccuVAC-D004\textsubscript{C} (Colon cancer)
Sipuleucel-T: The only FDA-approved DC cancer vaccine

HR = 0.775 (95% CI, 0.614, 0.979)  
\( P = 0.032 \) (Cox model)  
Median survival benefit = 4.1 months

Sipuleucel-T (n = 341)  
Median survival: 25.8 months  
36-mo. survival: 31.7%

Control (n = 171)  
Median survival: 21.7 months  
36-mo. survival: 23.0%

No. at risk  
Sipuleucel-T 341 274 129 49 14 1  
Control 171 123 55 19 4 1
The process of developing a DC vaccine

Where the Accum™ formulation is used
The AccuVAC-D001
Cancer vaccine leads to potent protection and sustainable memory response

A

10⁵ DCs (SC)  5 x 10⁵ EG.7  1 x 10⁶ EG.7  2 x 10⁶ EG.7
0  7  14  21  28  35  42  49  56  63  70  77  84

B

Tumor volume (mm³)

C

Percent survival
Therapeutic delivery of the AccuVAC-D001 leads to 70% cure in mice with pre-established tumors
AccuVAC-D001 mechanism of action in the tumor

1. AccuVAC-D001 Injection

2. Immune cell recruitment

3. Immune cell activation

4. Endogenous DC cross-priming

Allogeneic AccuVAC-D001 recruits and activates patients own immune cells

- CD8 T cells
- NK cells
- IFN-γ
- IL-6
- MIP-2
- MIP-1β
- αPD-1

Allo-DC
Melanoma Phase I trial (UK): 3+3 Design

Part A
AccuVAC-D002\textsubscript{M} Monotherapy
Dose Escalation 3+3 Design

- 5 x 10\textsuperscript{6} AccuVAC-D002\textsubscript{M}
- 10 x 10\textsuperscript{6} AccuVAC-D002\textsubscript{M}
- 15 x 10\textsuperscript{6} AccuVAC-D002\textsubscript{M}

Part B
AccuVAC-D002\textsubscript{M} + anti-PD-1

- 10 x 10\textsuperscript{6} AccuVAC-D002\textsubscript{M}
INTRODUCING THE ADC PROGRAM:
Pre-clinical proof of concept

AccuADC-001 (Breast and gastric cancers)
AccuADC-002 (Breast and gastric cancers)
What is an Antibody-Drug Conjugate (ADC)?

Examples:
- Brentuximab (CD30 - HL)
- Trastuzumab (HER2 - Breast cancer)
- Inotuzumab (CD22 - ALL)
- Gemtuzumab (CD33 - AML)

Examples:
- Monomethyl auristatin (MMA)
- N2‘-Deacetyl-N2’-(3-mercapto1-oxopropyl)-maytansine (DM1)
- Calicheamicin

Examples:
- Maleimidomethyl cyclohexane1-carboxylate (MCC)
- Maleimidocaproyl-valine citrulline (MC-VC)
- 4-(4-acetylphenoxy)butanoic acid (AcBut)
Accum™ Enhances Therapeutic Potency of Trastuzumab-DM1 (AccuADC-001)

Accum™ increase potency of uncleavable Kadcyla® ADC by 10-100 folds

Accum™-Kadcyla® induces superior tumor regression compared to Kadcyla®

Single ADC injection at 3mg/kg in orthotopic JIMT-1 breast cancer cell in mice
Further Enhancing Our ADC program

Screening of ACCUM™ variants with Trastuzumab-DM1 ADC (Kadcyla®)

**JIMT-1 breast cancer**

**Ongoing Steps: 8 best Accum™ variants**

- Defence Therapeutics Inc. has established a collaboration with the HUS Comprehensive Cancer Center in Helsinki, Finland, for the optimization of Defence's Accu-T-DM1 ADC therapeutic
- Defence Therapeutics Inc. has established a collaboration with the Curie Institute (Paris, France) to evaluate the therapeutic efficacy of Accu-T-DM1 ADC in patient-derived xenograft (PDX) models of breast cancer
Competitors in the Field
INTRODUCING THE AccuTOX PROGRAM
Pre-clinical proof of concept

AccuTOX-001_L
AccuTOX-002_B
accum™ Enhances antigen uptake when chemically linked, but...

Accum-Antigen +

Accum + Antigen +
AccuTOX-001L can be leveraged as an anti-cancer therapeutic with a wide scope of action.
Intra-tumoral delivery of AccuTOX-001 delays tumor growth as a stand-alone therapy

A GLP study is currently ongoing
Breast Cancer Phase I trial (Canada): 3+3 Design

Part A
AccuVAC-D002\textsubscript{M} Monotherapy Dose Escalation 3+3 Design

- 0.5 mg/kg AccuTOX-002\textsubscript{B}
- 1 mg/kg AccuTOX-002\textsubscript{B}
- 5 mg/kg AccuTOX-002\textsubscript{B}

Part B
AccuVAC-D002\textsubscript{M} + T-DM1

- 1 mg/kg AccuVAC-D002\textsubscript{M}
INTRODUCING THE COVID (ID) VACCINE PROGRAM:
Pre-clinical proof of concept

AccuVAC-PT001
AccuVAC-IN002
AccuVAC-PT001
Induces strong, long-lasting and neutralizing humoral responses
AccuVAC-PT001-induced antibodies cross-react with all tested variants

A challenge study in hamsters is currently ongoing
A GLP study is scheduled for Q1 of 2022 for the injectable vaccine.
Intranasal delivery of AccuVAC-IN003 triggers both mucosal and systemic humoral responses
AccuVAC-IN003 induces a panoply of pro-inflammatory mediators

A GLP study is currently ongoing for IN Vaccination
## Competitive advantage in the Field

<table>
<thead>
<tr>
<th>Technology Platforms</th>
<th>DTC”s AccuVac-IN003</th>
<th>RNA</th>
<th>DNA</th>
<th>Viral Vectors</th>
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<tbody>
<tr>
<td>Expected No. of doses</td>
<td>1 to 2</td>
<td>2 to 3</td>
<td>2</td>
<td>1 to 2</td>
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<tr>
<td>Route of Administration</td>
<td>Intransal spray</td>
<td>Injection</td>
<td>Injection + Electroporation</td>
<td>Injection</td>
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<tr>
<td>Mucosal Immunity</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
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<tr>
<td>Stability</td>
<td>√√√√</td>
<td>√</td>
<td>√√√</td>
<td>√√√</td>
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<tr>
<td>Ease of Use</td>
<td>√√√√</td>
<td>√√√</td>
<td>√</td>
<td>√√√</td>
</tr>
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</table>
INTRODUCING THE HPV VACCINE PROGRAM:
Discovery Stage

AccuVAC-PT004
Current HPV vaccines are great, but not perfect!

According to the CDC, the HPV vaccination decreased rates of infection with HPV in half in American teenagers (from 11.5% to 4.3%) and by one third in American women in their early twenties (from 18.5% to 12.1%)

Remain ineffective against HPV types 31, 33, 35, 39, 45, 51, 52, 56, 58, and 59 – **Gardasil-9 covers** HPV types 6, 11, 16, 18, 31, 33, 45, 52, and 58

Used prophylactically (before infection), not as a therapeutic vaccine (post-infection/cervical cancer appearance)

There is still room for improvement

The global HPV Vaccine market size was valued at $3.80 Bn in 2019 and is projected to reach $12.69 Bn by 2027 with a CAGR of **16.3%**
Our Proposed Strategy

Current Strategy

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>Gardasil 9</th>
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<tbody>
<tr>
<td>AAHS (aluminum adjuvant)</td>
<td>500 mcg</td>
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<tr>
<td>Sodium Chloride</td>
<td>9.56 mcg</td>
</tr>
<tr>
<td>L-Histidine</td>
<td>.78 mcg</td>
</tr>
<tr>
<td>Polysorbate 80</td>
<td>50 mcg</td>
</tr>
<tr>
<td>Sodium Borate</td>
<td>35 mcg</td>
</tr>
<tr>
<td>Yeast Protein</td>
<td>&lt;7 mcg</td>
</tr>
<tr>
<td>HPV 6 L1 protein</td>
<td>30 mcg</td>
</tr>
<tr>
<td>HPV 11 L1 protein</td>
<td>40 mcg</td>
</tr>
<tr>
<td>HPV 16 L1 protein</td>
<td>60 mcg</td>
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<tr>
<td>HPV 18 L1 protein</td>
<td>40 mcg</td>
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<td>HPV 31 L1 protein</td>
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<td>HPV 45 L1 protein</td>
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<tr>
<td>HPV 52 L1 protein</td>
<td>20 mcg</td>
</tr>
<tr>
<td>HPV 58 L1 protein</td>
<td>20 mcg</td>
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</table>

‘Empty’ non-infectious virus-like particle (VLP) mimics the virus

Defence Strategy

A mix of chemically-linked L1 proteins to Accum

- HPV 6
- HPV 11
- HPV 16
- HPV 18
- HPV 31
- HPV 33
- HPV 45
- HPV 52
- HPV 58

Making a Global Impact  | Defence Therapeutics
Competitors in the Field

**Prophylactic Vaccination**

- CERVARIX
- GARDASIL
- GARDASIL 9

**Therapeutic Vaccination**

- VGX-3100 (DNA Vaccine in Phase III)
Overall Summary

Accum™ molecule

Bile acid  NLS

Highly Versatile Technology

Enhance significantly the therapeutic potency of DC vaccines
Augment the anti-tumoral potency of FDA-approved ADCs
Easily applicable to ID protein-based vaccines (eg COVID/HPV)
Development of novel small molecules with anti-cancer properties (New ADC opportunity)
Thank You

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