

Croda Pharma

ADJUVANTS

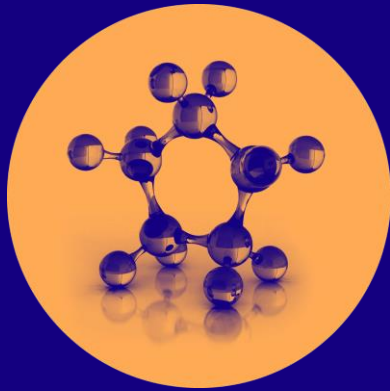
THE TOOL TO OBTAIN THE REQUIRED IMMUNE RESPONSES IN PROPHYLACTIC AND THERAPEUTIC VACCINATION

Dennis Christensen, PhD,
Head of Global R&D, Adjuvant systems

Smart science to improve lives™

CRODA

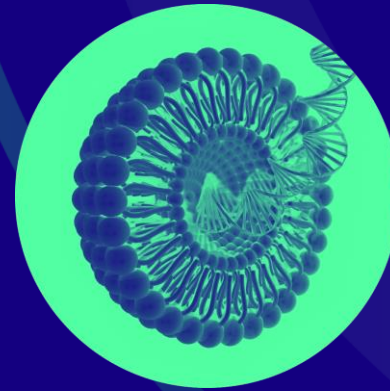
Croda Pharma platforms



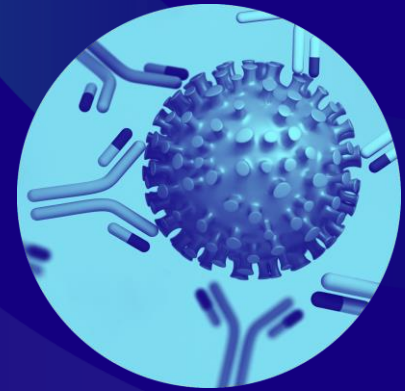
**Small Molecule
Delivery**



**Protein
Delivery**



**Nucleic Acid
Delivery**



**Adjuvant
Systems**

Human and Veterinary Health

Our journey to Croda Pharma

1925

Croda was founded



2000 onwards

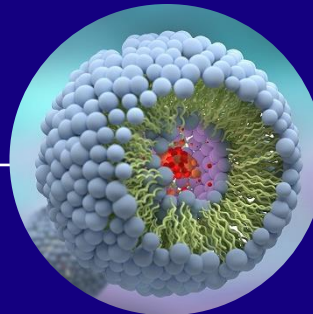
Ongoing investments in high purity excipients



2020



Acquisition of world leading lipid portfolio



2018

Biosector acquisition, industry leading vaccine adjuvants



2021

Global investments in pharma +£100m – a commitment to advancing expertise



2022

Our Health Care business becomes

Croda Pharma



Croda Pharma Adjuvant Systems R&D goals

- To be the “go-to” partner for human vaccine companies
- To design and develop vaccine adjuvant systems for any purpose needed
- To design adjuvant systems, where supplies are not at risk
- To bring forth safe and effective adjuvant systems to the world



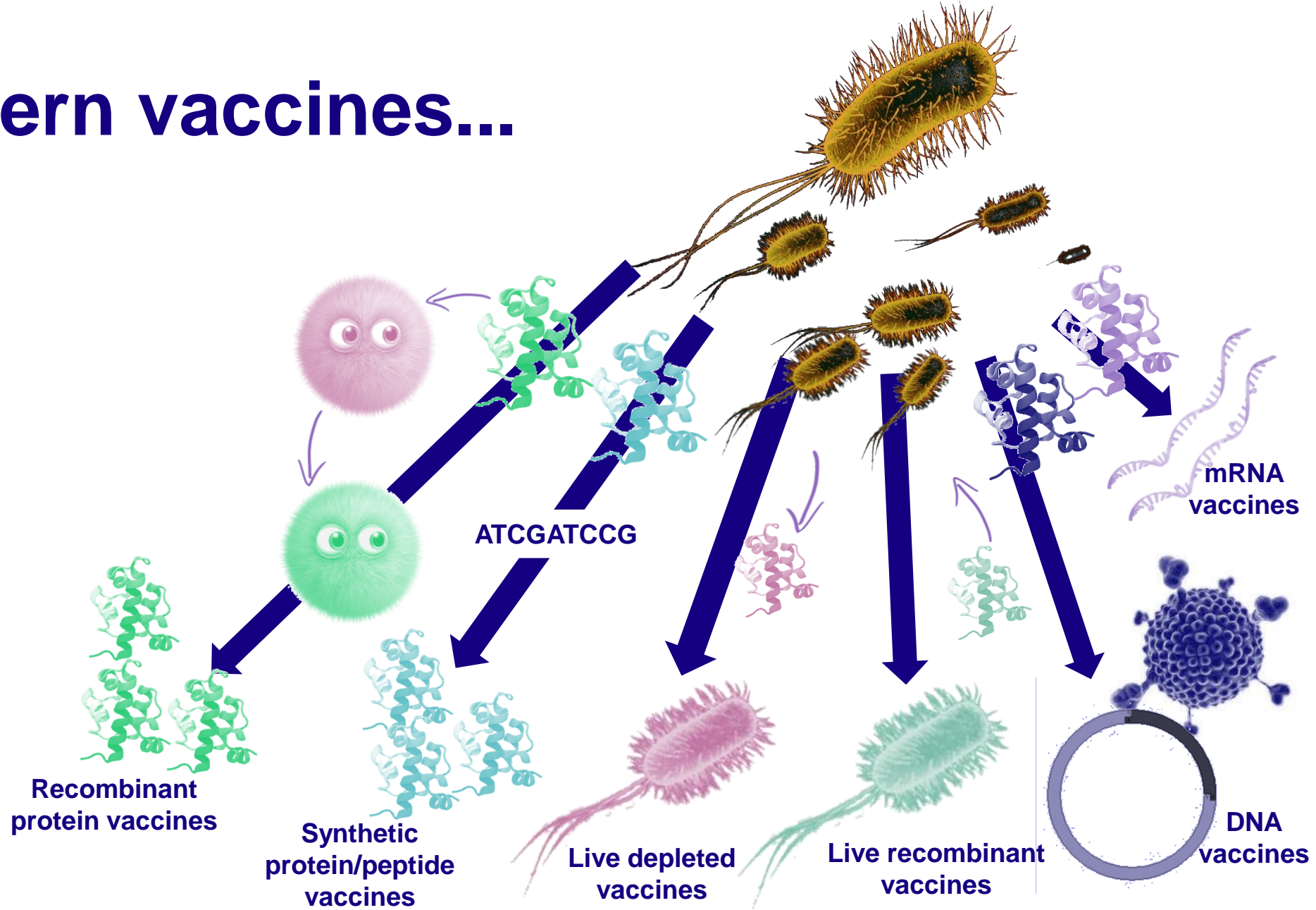
Modern vaccines



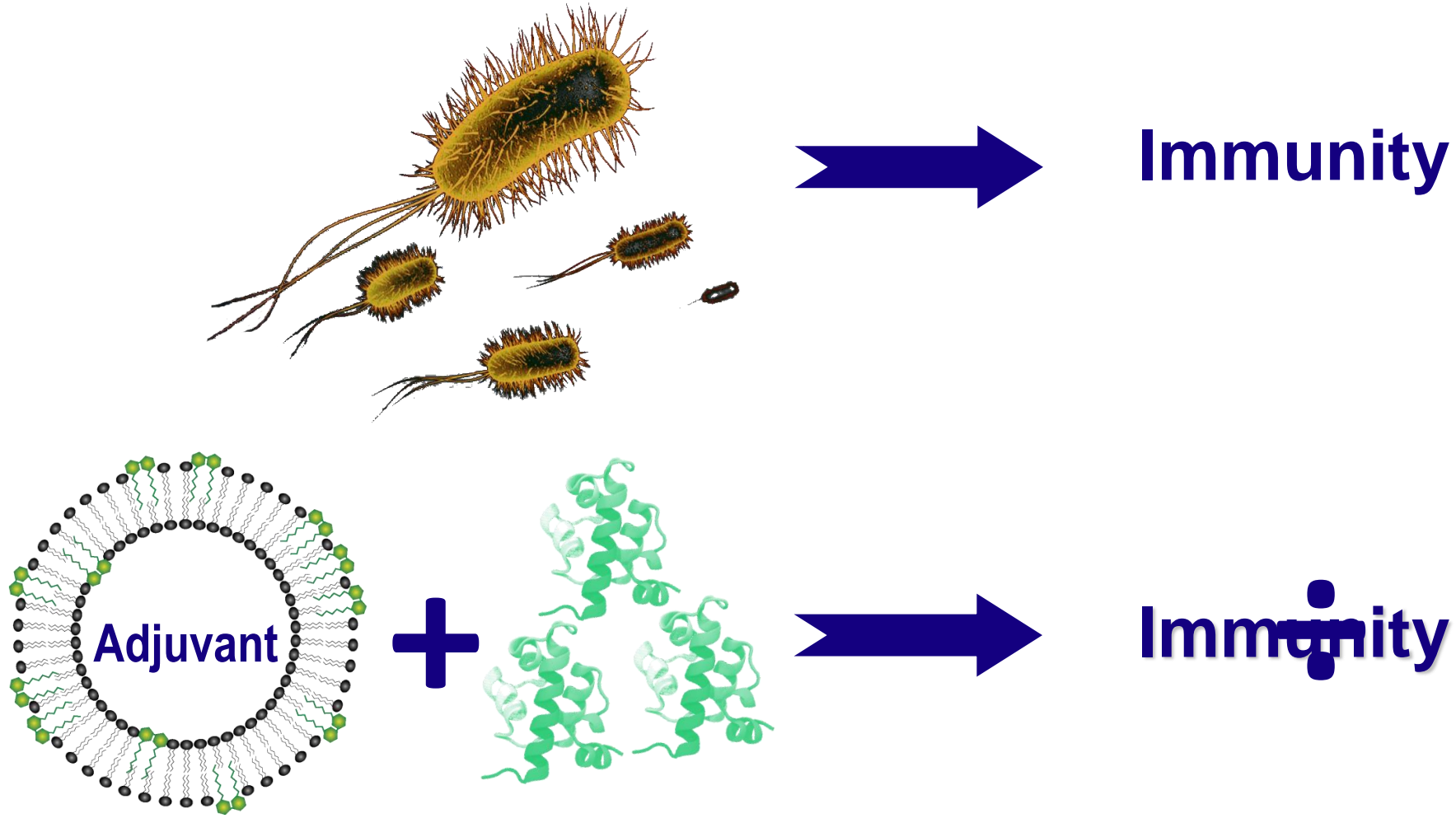
Vaccination is all about

1. Presenting **sufficient amounts** of the **right antigen**
2. In the **right conformation**
3. To the **right cell** populations
4. While supporting with the **right co-stimuli**
5. For a **sufficient amount of time**

Modern vaccines...



Modern vaccines vs old...



Modern vaccines

Delivery system

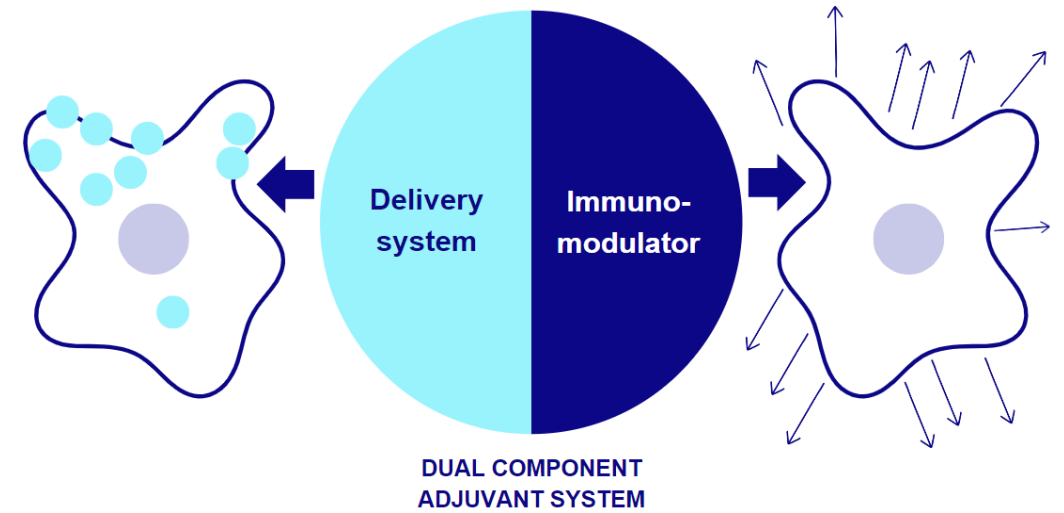
compositions facilitating delivery of antigen and immunomodulators to the right cells

Immunomodulator

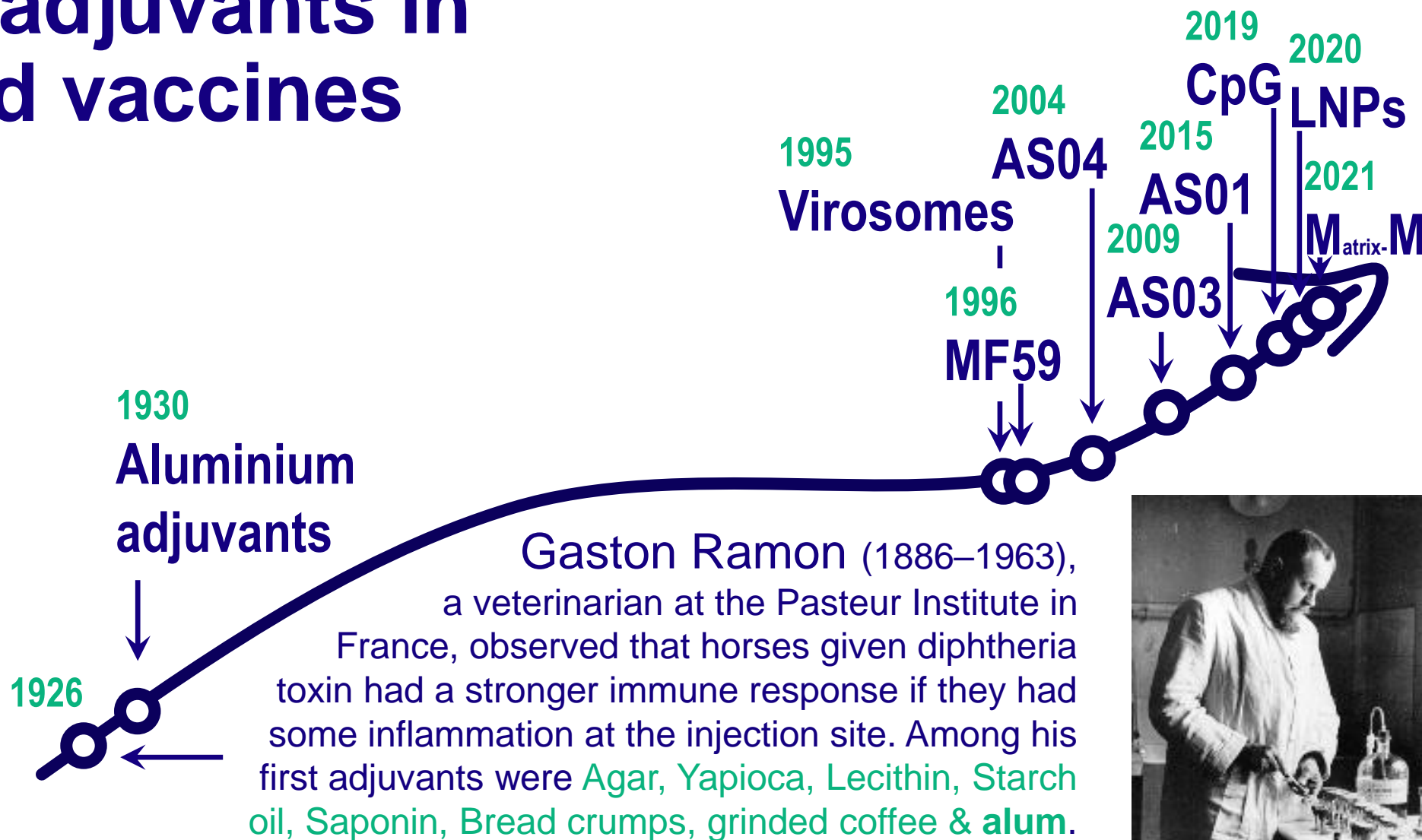
compounds having a specific modulating/stimulating effect on the immune system affecting the flavour/strength/duration of the immune response

Antigen

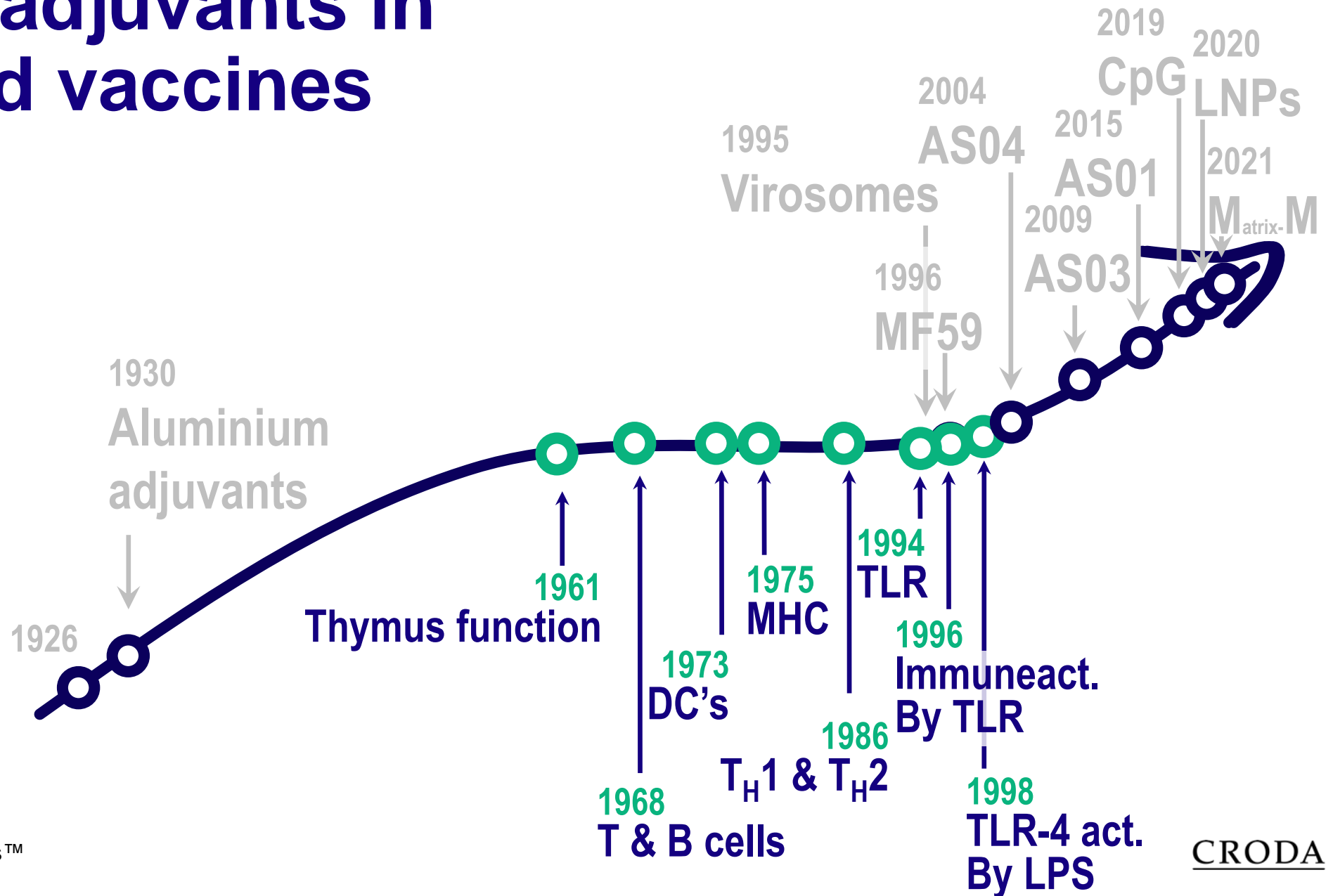
a molecule or molecular structure or any foreign particulate matter that can bind to a specific antibody or T-cell receptor



Vaccine adjuvants in approved vaccines



Vaccine adjuvants in approved vaccines



Croda Pharma

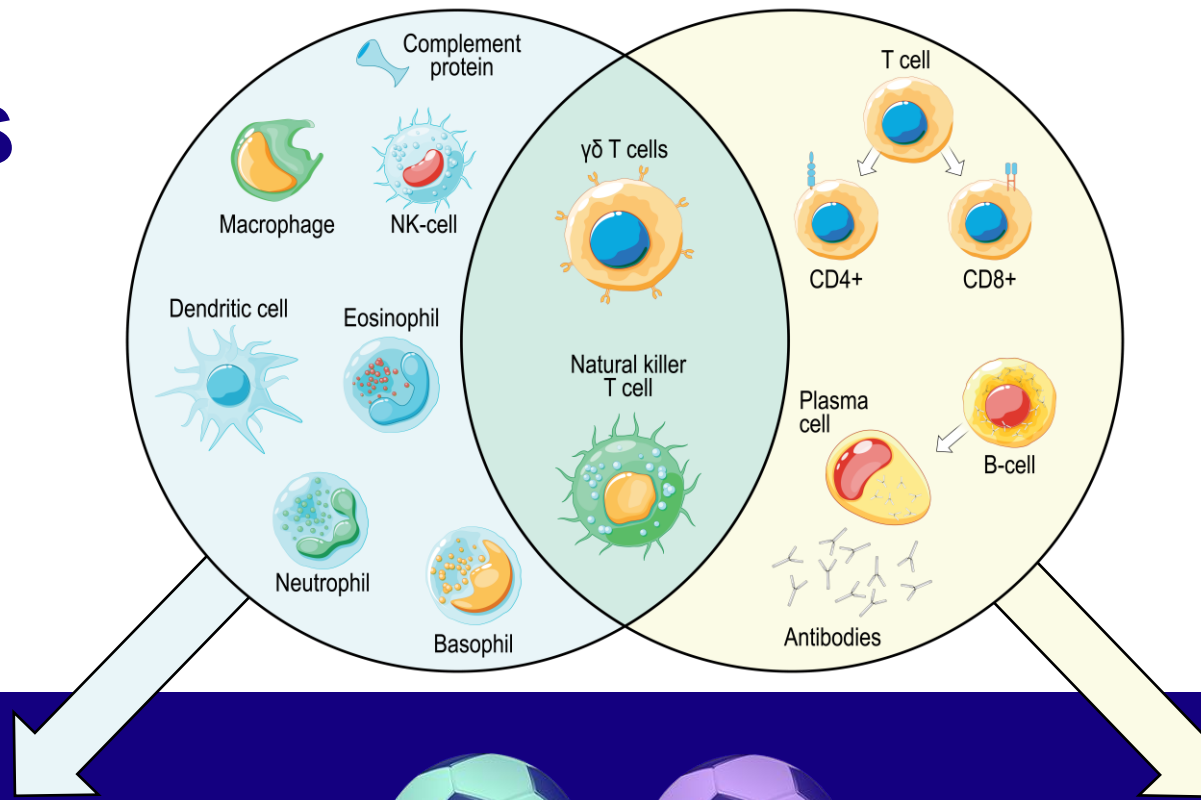
The Immunomodulator



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The actors

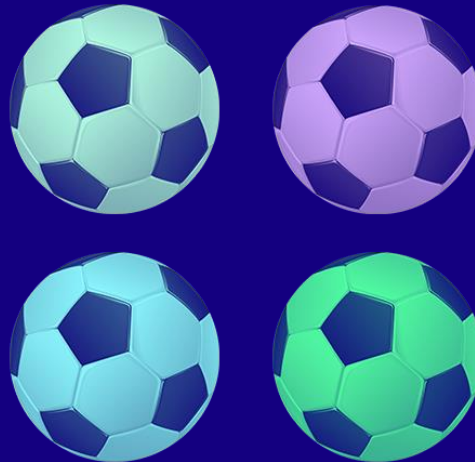


INNATE IMMUNE SYSTEM

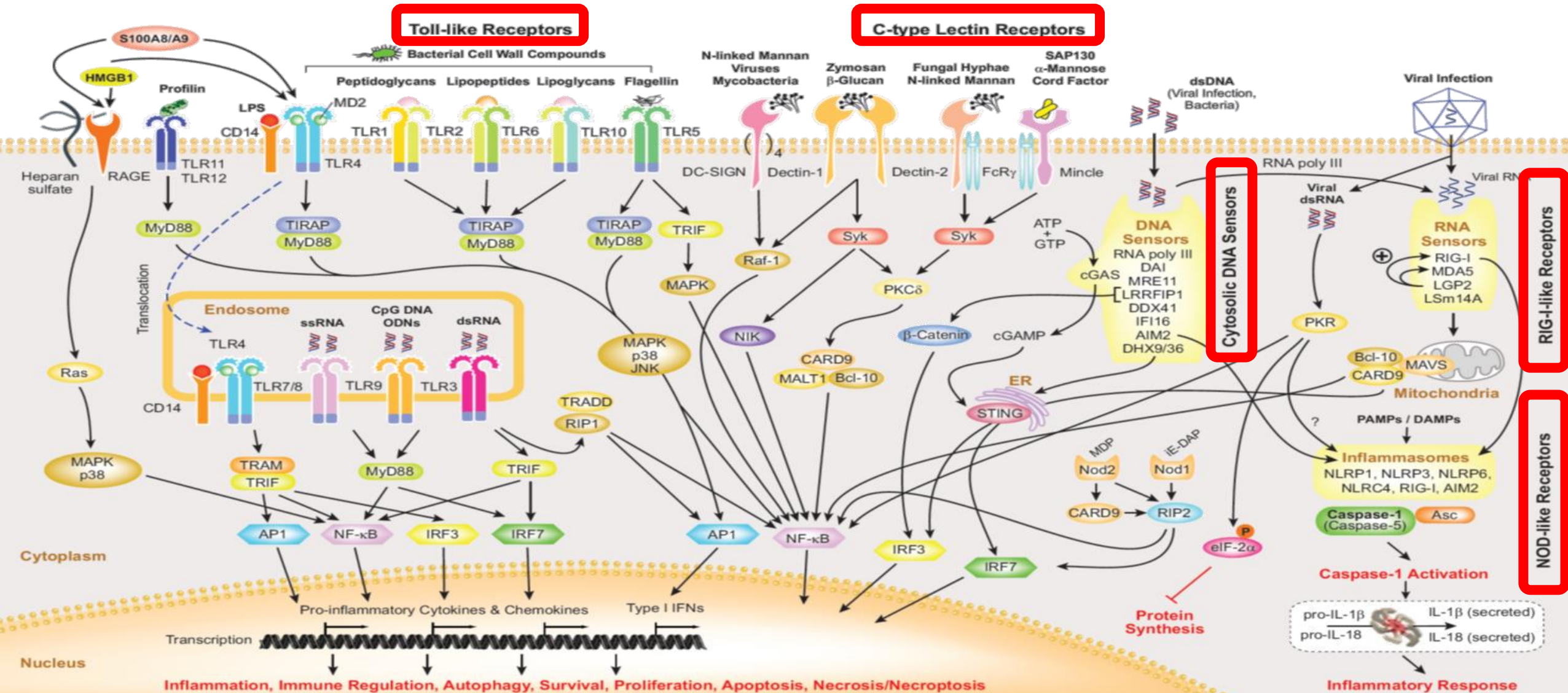
- Recognises general patterns on the pathogen – **THE DARK FIELDS**
- Reacts with full power
- Induces disease symptoms
- Presents unique patterns (antigens) to the adaptive immune system

ADAPTIVE IMMUNE SYSTEM

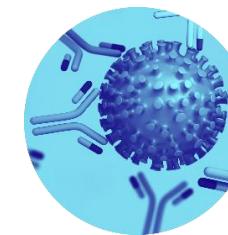
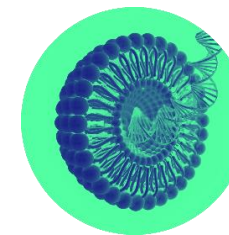
- Recognises unique patterns on the pathogen – **THE COLOURED FIELDS**
- Reacts controlled and specifically
- "No" symptoms
- Stored in immunological memory



Immunomodulatory targets (PRRs)



Croda Immunomodulators



From research to GMP grade supply

Mineral
adjuvants

Alhydrogel™
Adju-Phos™

Liposomal
adjuvant
systems

CAF®01
CAF®09b

Lipids

Phospholipids
Cationic lipids
PEG lipids
Structural lipids
Plant-based cholesterol

Saponin
adjuvants

NanoQuil™

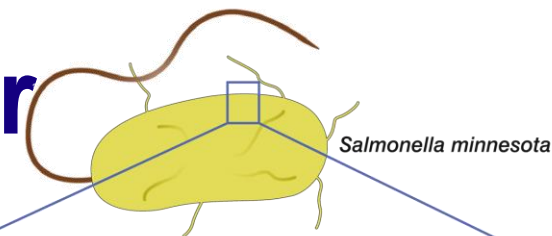
Immuno-
modulators

PHAD™
3D-PHAD™
3D-(6-acyl)-PHAD™
TDB
QS-21

Other
components

Super Refined™
Polysorbate 80 and 20
Span™ 85 Pharma

From PAMP to immunomodulator



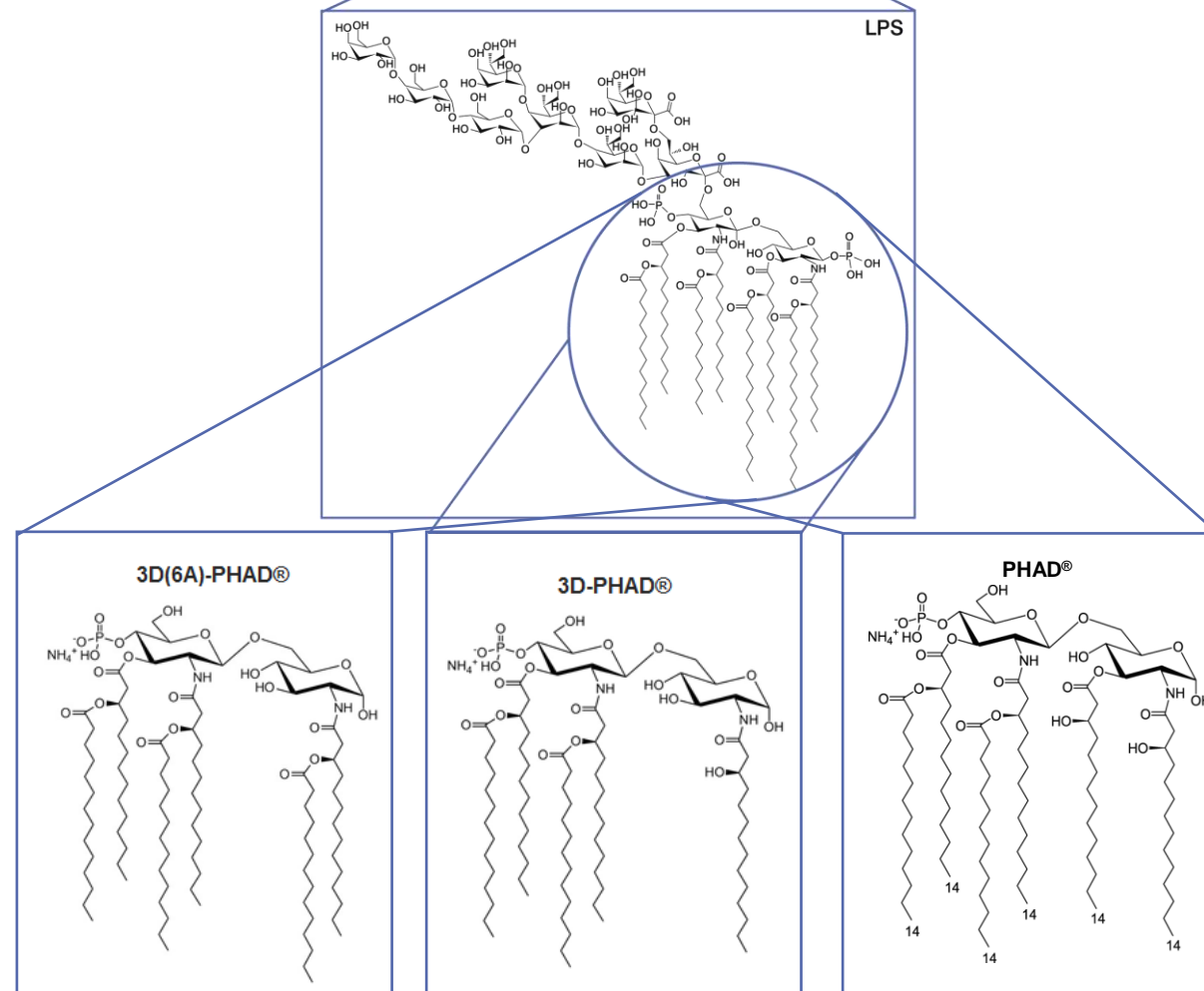
Lipopolysaccharide (LPS)

- Component of the outer membrane of gram-negative bacteria
- Contributing to the structural integrity of the bacteria
- Induces a strong response from normal animal immune systems targeting several PRRs including TLR2 and 4

Phosphorylated HexaAcyl Disaccharide (PHAD)

- Fully synthetic equivalent to bacterial-derived monophosphoryl lipid A
- TLR4 agonist inducing Th1 responses
- 3 types available in GMP quality
 - PHAD (also referred as GLA)*
 - 3D-PHAD
 - 3D(6-acyl)-PHAD

*proven safety and tolerability in >30 clinical trials



Croda Pharma

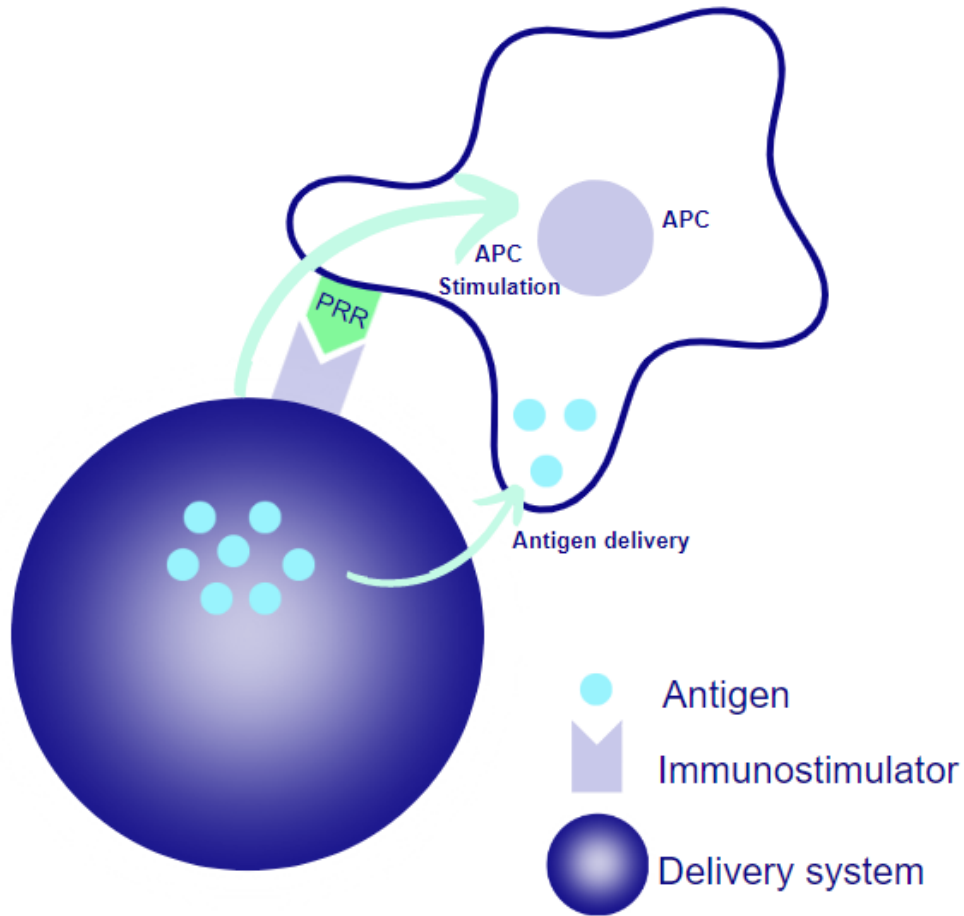
The delivery system



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Vaccine delivery properties



- Vaccines typically contain multiple modalities

- Antigen modalities

- Proteins
- Peptides
- DNA
- Split components
- Whole inactivated pathogens
- Etc.

- Immunomodulator modalities

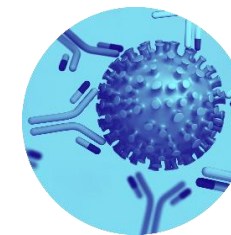
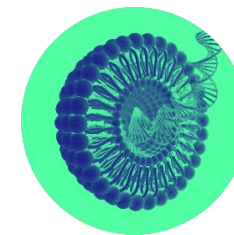
- Lipids (MPL, TDB, MMG, PDIM etc)
- Proteins (CTB, CTA, DT)
- Peptides (MDP)
- DNA (CpG motifs)
- RNA (poly IC)
- Small molecules (Resiquimod, Imiquimod etc)
- Etc.

Delivery system

- Liposomes
- ISCOMS
- o/w emulsions
- w/o emulsions
- polymer micro- and nanoparticles
- Gels
- Crystals
- Salts
- Cubosomes
- Hexosomes
- Etc.



Croda Components for delivery systems



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CAF®09b

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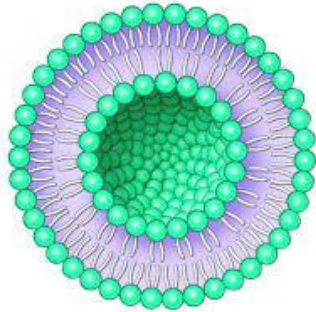
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3D-PHAD™
3D-(6-acyl)-PHAD™
TDB
QS-21

Other
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Span™ 85 Pharma

GMP components for adjuvant delivery & formulation

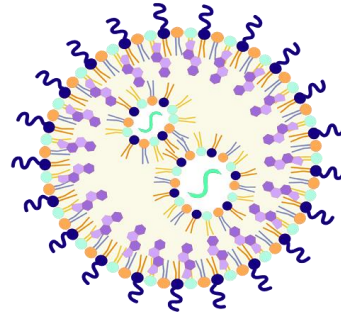
Liposomes



GMP lipids for liposomes

- DSPC
- DMPC
- DMPG
- Plant-based cholesterol (EP2397)

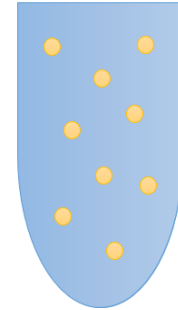
Lipid nanoparticles



GMP lipids for LNPs

- DOTAP
- DMG-PEG2000
- DSPE-PEG2000
- DSPC
- DOPE
- Plant-based cholesterol (EP2397)

Emulsions

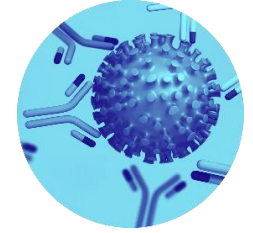
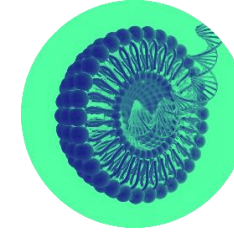


High purity excipients

- Super Refined Polysorbate 80
- Super Refined Polysorbate 20
- Span 85 Pharma

The Croda Adjuvant Systems

A unique portfolio for vaccine development



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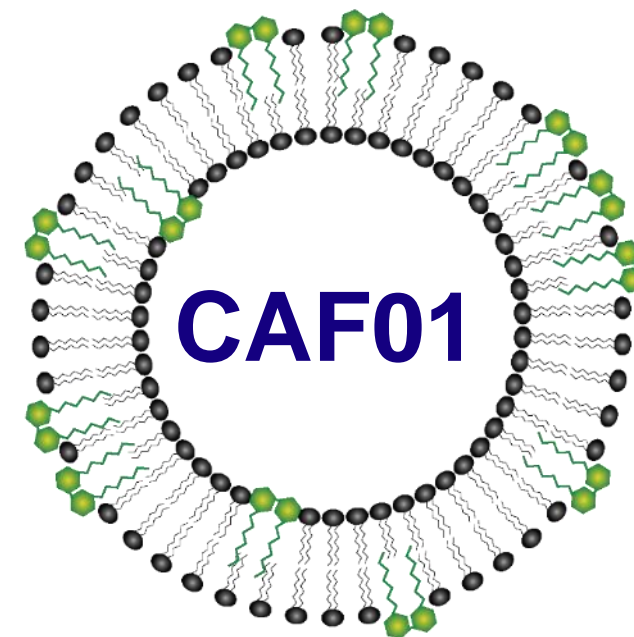
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CAF[®]01

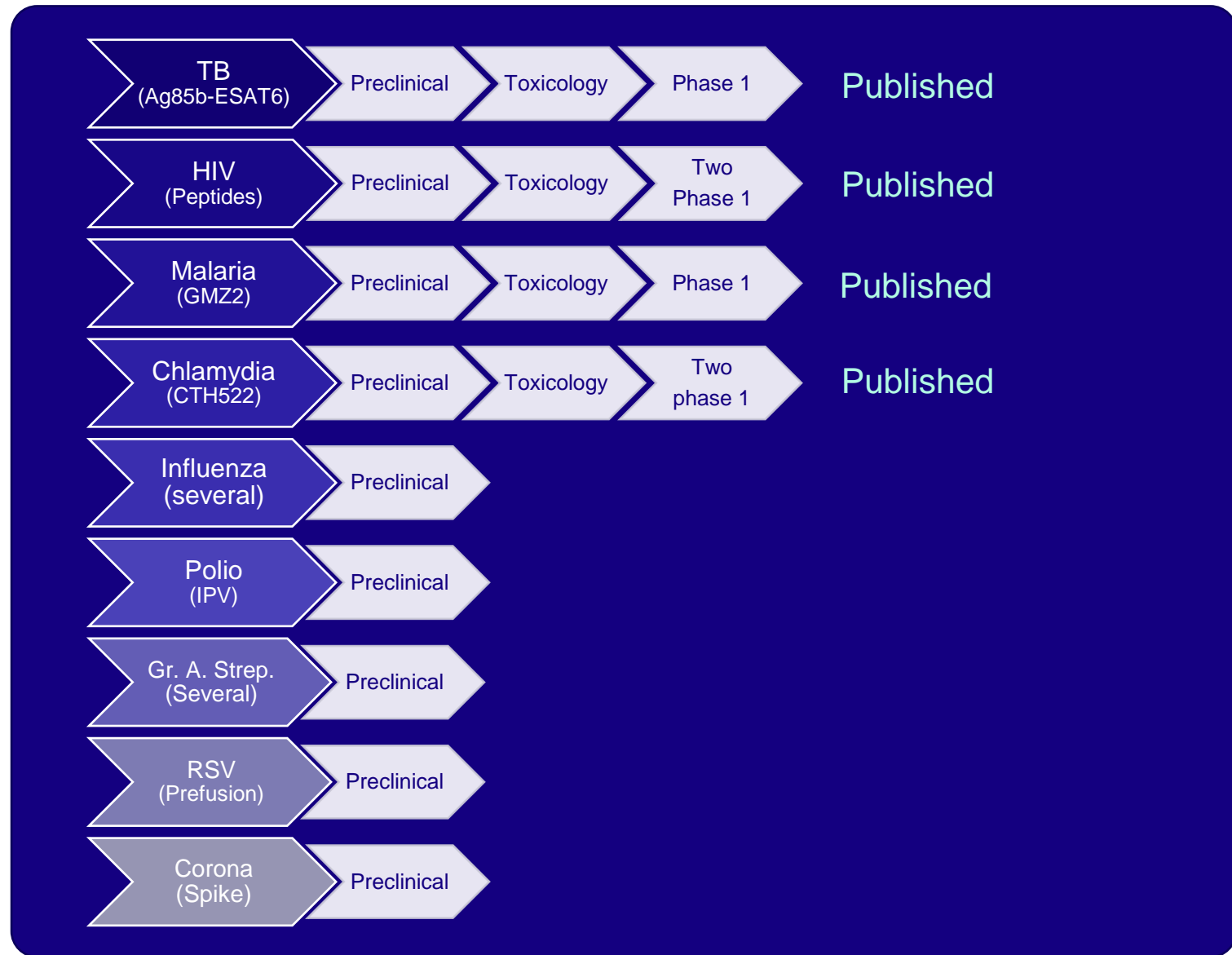
A two-component liposomal suspension composed of dimethyldioctadecylammonium (**DDA**) and C-type lectin receptor agonist trehalose dibehenate (**TDB**).

- A fully synthetic cationic liposomal adjuvant formulation that drives both humoral and cellular immune response in combination with eg protein- and peptide-based antigens
- Elicits potent antigen-specific T-cell responses (Th1/Th17)
- Excellent long-term stability
- Proven safety and tolerability, no residual tissue damage, no injection site nodule formation



Status CAF01

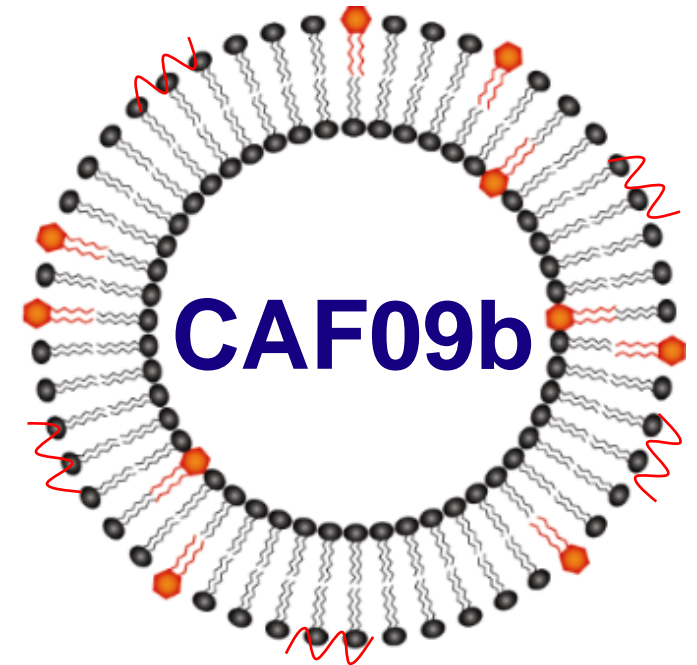
- 6 finalised phase 1 CT
- 4 different antigens
- Strong Th1/Th17 and antibody responses



CAF[®]09b

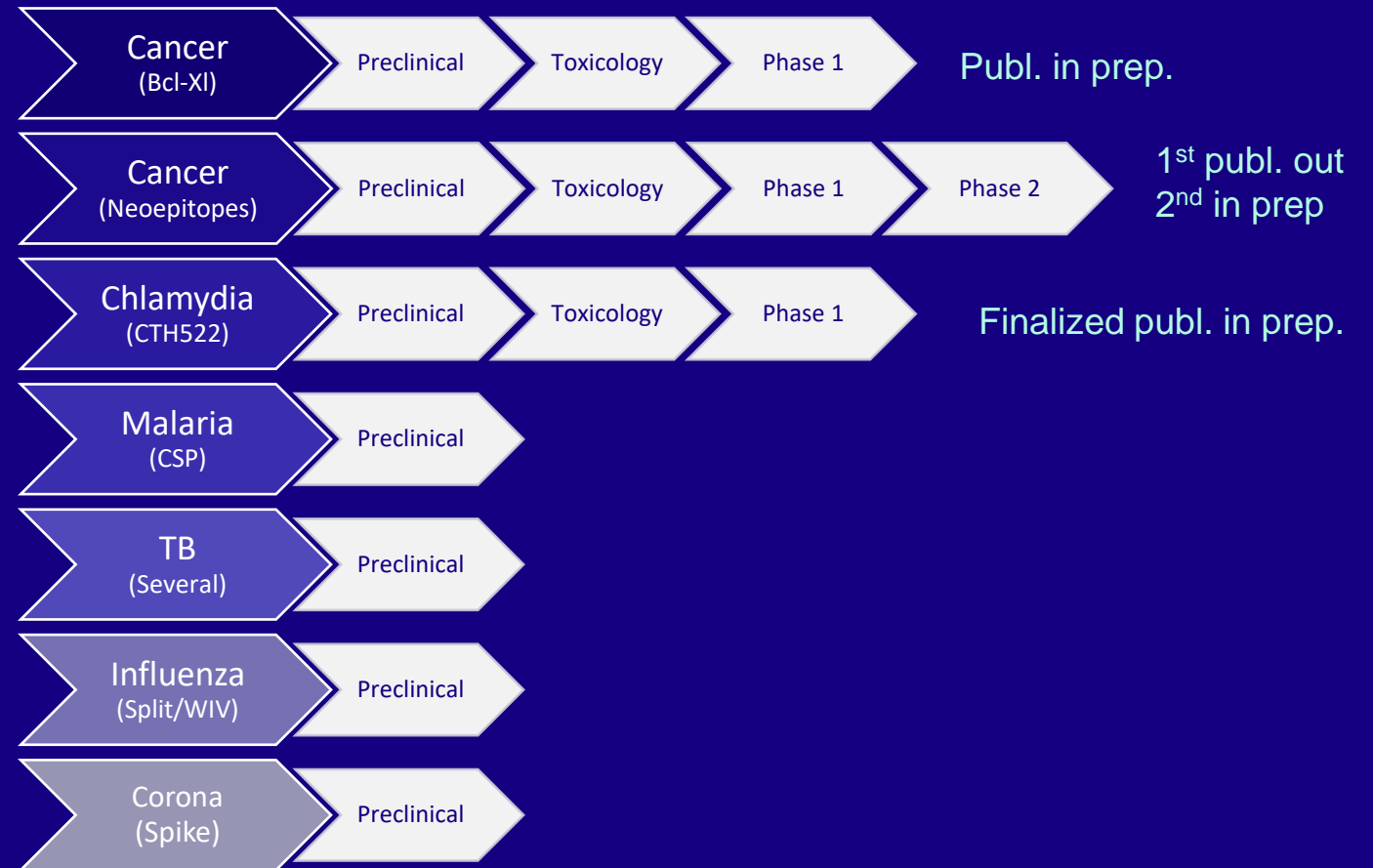
A three component liposomal suspension based on **DDA** combined w. CLR agonist monomycoloyl glycerol (**MMG**) and TLR3 agonist **poly I:C**

- A fully synthetic cationic liposomal adjuvant formulation that drives strong CD8 T-cell responses after vaccination in combination with eg peptide- or protein-based antigens
- Proven safety and better tolerability in comparison to poly I:C
- Early stage studies indicate it could be a potential adjuvant for mucosal applications



Status CAF09b

- 3 finalized phase 1 CT
- 1 ongoing phase 2 CT
- Cancer trials: TAA and neoepitopes
 - i.p. + i.m. vaccinations
 - Strong Th1 and CTL responses
- Chlamydia trial: CTH522
 - i.m. vaccinations





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We are actively pursuing new partnerships

- We **are** specialists in vaccine adjuvant research, development and production
- We **will** engage in vaccine programs with collaborators from **academia** to **big pharma**
- We **do** supply highest quality products for pre-clinical and clinical development programs
- We **perform** custom vaccine Ag+Adjuvant formulation development
- We **perform** characterization of vaccine Ag+Adjuvant formulations
- We **ensure** adjuvant supply from research to final product

Smart science to improve lives™



CRODA

Thank you!

Dennis Christensen, PhD

dennis.christensen@croda.com



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