

**s**  **n m e d i x**

Next Generation Antibiotics

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Recent global study found that drug-resistant bacterial infections were associated with almost **5 million deaths** in 2019.

(The Lancet, Jan 2022)

The  
Economist

MAY 21ST - 27TH 2018

Do recoveries die, or are they killed?  
Pinstriped greens take on Big Oil  
Boss of the UN: worst job in the world  
Win or lose, dark days for Cameron  
How gangs suck El Salvador dry

## When the drugs don't work

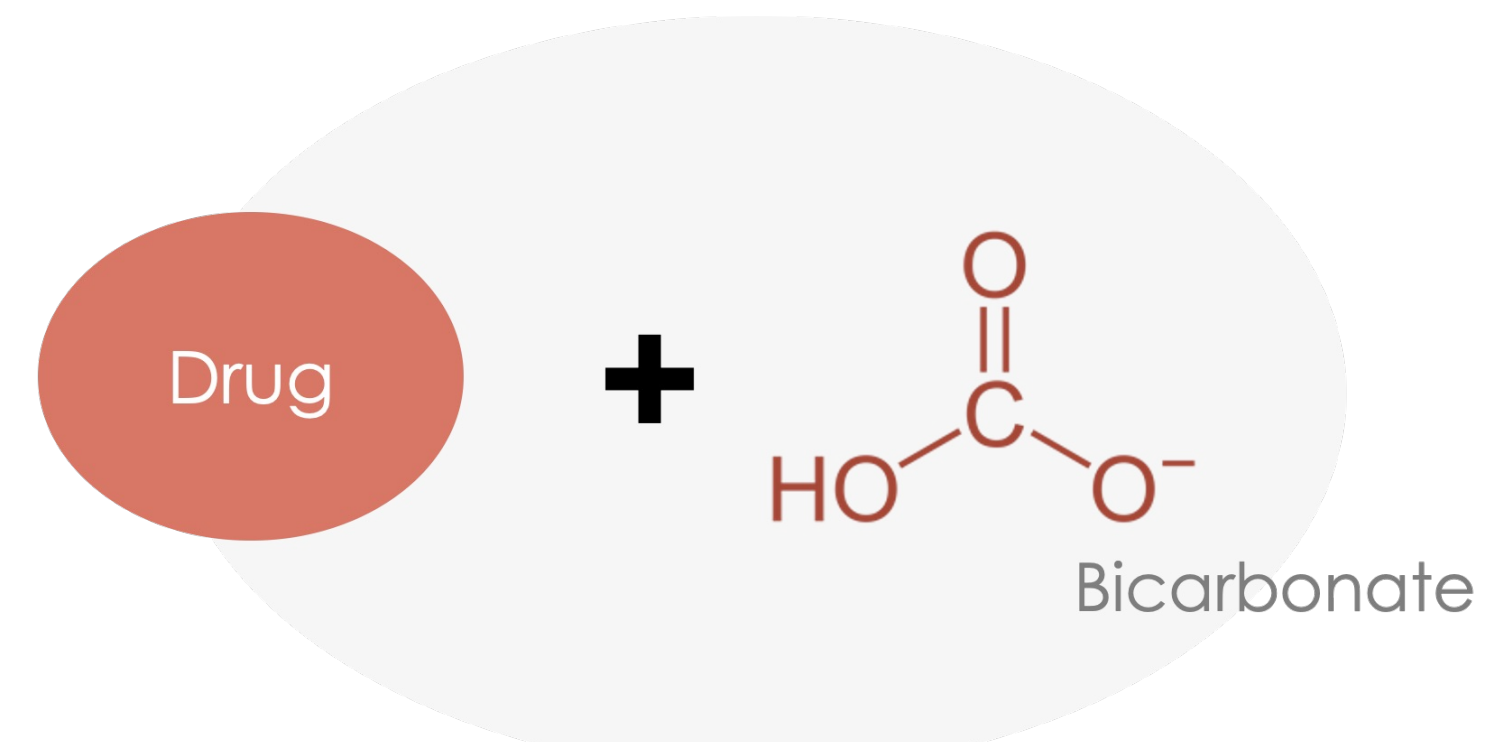
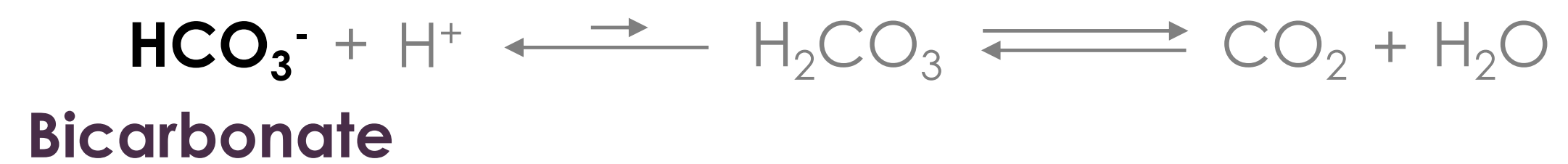
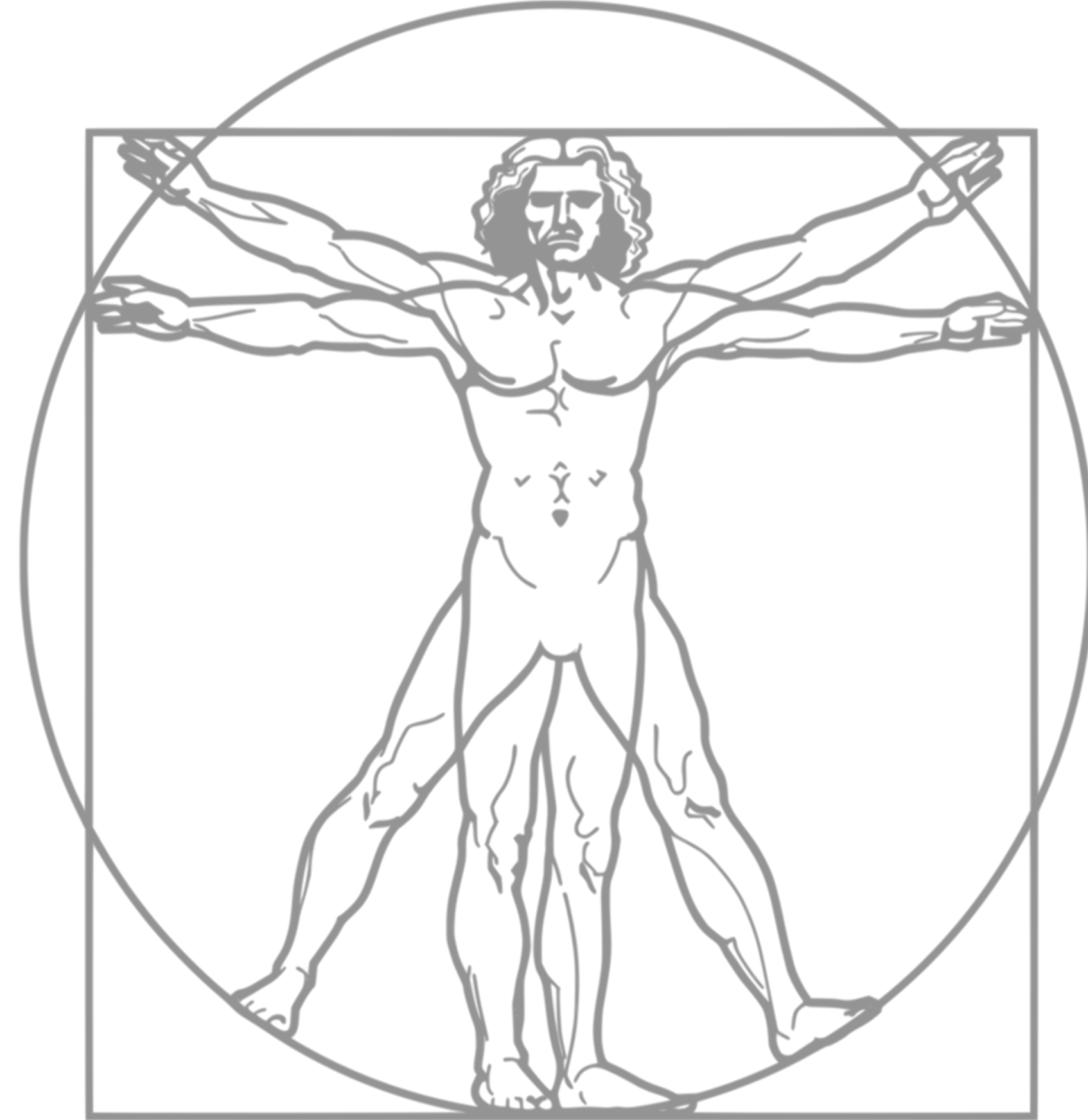
**The rise of antibiotic resistance**



# THE DISCOVERY

Our body's bicarbonate buffer system enhances the action of many antibiotics and our innate immune system.

This *bicarbonate effect* can be exploited to develop *next generation antibiotics*.





A strong **patent** portfolio around the use of bicarbonate for **synergistic** antibiotic action.

## Composition and Use

### Bicarbonate + Azithromycin

**Granted**

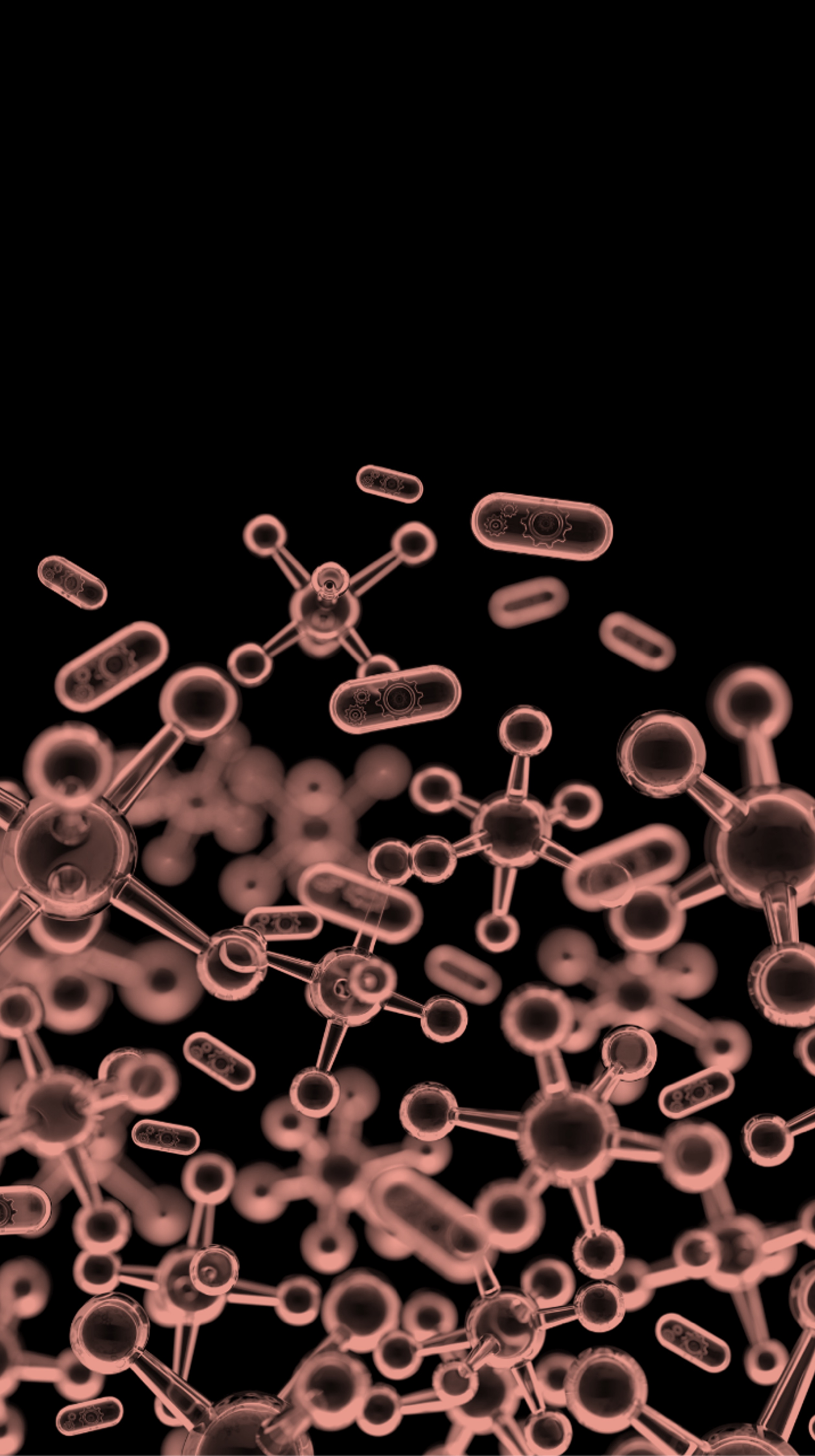
U.S. Patent Application No. 62/713,231  
U.S. Patent No: 10,940,163 B2

## Composition and Use

### Bicarbonate + Bioactives

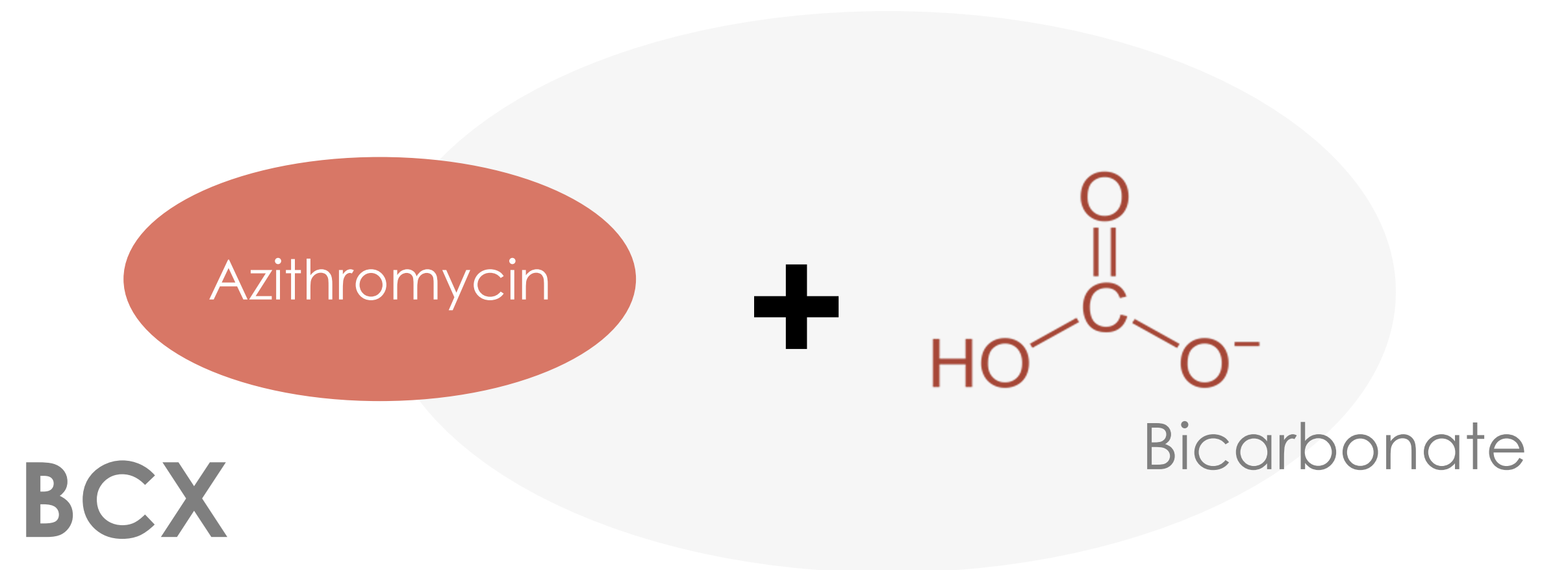
**Granted**

U.S. Patent Application No. 15/887,469  
U.S. Patent No: unpublished

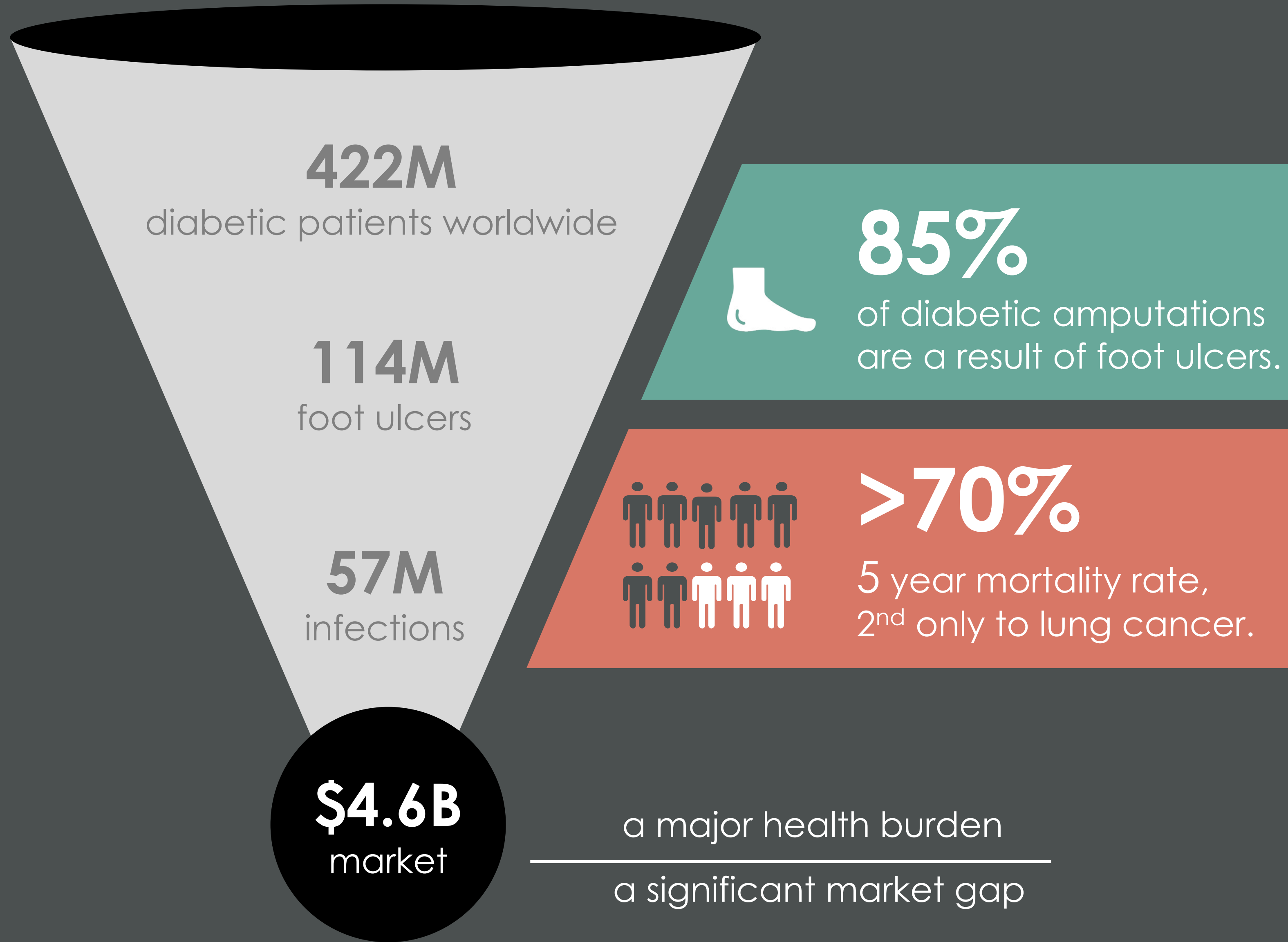


## PRIORITIZING TARGET INDICATIONS

- ✓ **LIMITED GENERIC COMPETITION**
- ✓ **INTELLECTUAL PROPERTY**
- ✓ **LOCAL THERAPY**



# OUR FIRST INDICATION: DIABETIC FOOT ULCER INFECTION



Despite the immense need  
**no therapies are approved**

The **International Working Group on Diabetic Foot** has issued a call for validated **topical antibiotics**.

# SYNMEDIX IS POISED TO DELIVER THE FIRST ANTIBIOTIC APPROVED FOR DFUI

## BCX – BICARBONATE + AZITHROMYCIN TOPICAL FORMULATION



### POTENT EFFICACY

CONTROL OF BACTERIAL GROWTH PROMOTES HEALING.



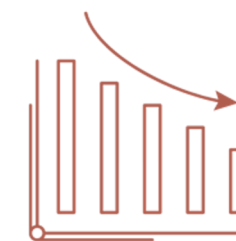
### REDUCE SIDE EFFECTS

PREVENT DEPLETION OF MICROFLORA AND SIDE EFFECTS.



### ACCELERATED APPROVAL

505 (B) (2) REGULATORY PATHWAY



### REDUCE TREATMENT COST

AVOID COMPLICATION, AMPUTATION AND LONG TERM CARE.



### PREMIUM PRICING

FIRST-IN-CLASS THERAPY, FIRST REIMBURSED OPTION



### MARKET EXCLUSIVITY

>10 YEARS



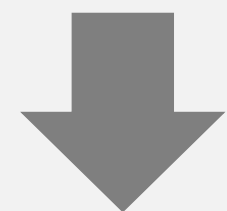
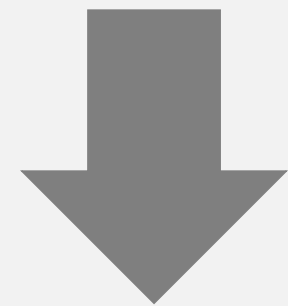
# OTHER INDICATIONS...

PRIORITIZING **CHRONIC WOUNDS** WHERE TOPICAL THERAPIES COULD BE GAME-CHANGING

- **Venous leg ulcers (\$2.9B market)**
- **Burn care (\$4.2B market)**
- **Blast wounds**
- **Lung infections (\$35.6B market)**

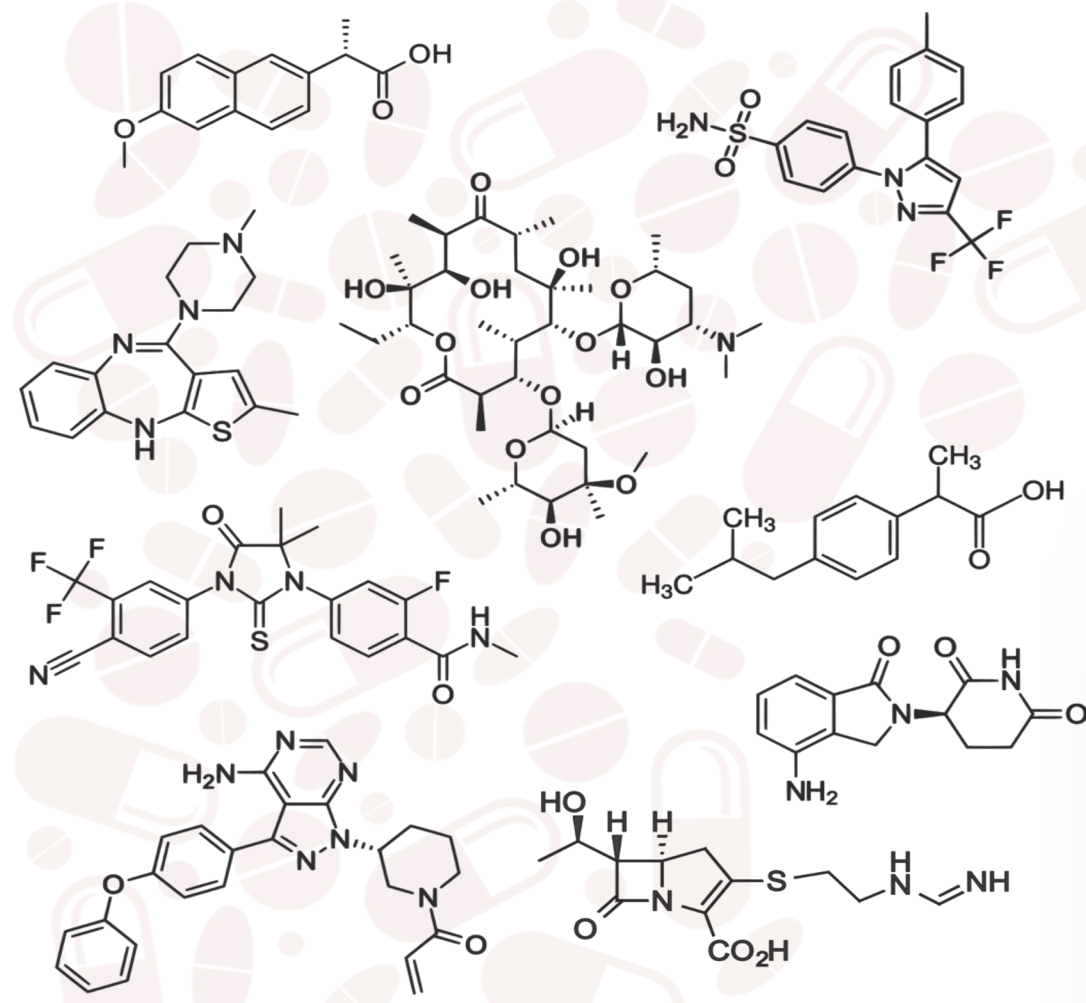
# AI DESIGN OF NOVEL DRUGS OPTIMIZED TO LEVERAGE THE BICARBONATE EFFECT

McMaster's chemical file  
diverse synthetic  
compounds



Hundreds of compounds  
enhanced by bicarbonate

Training Data

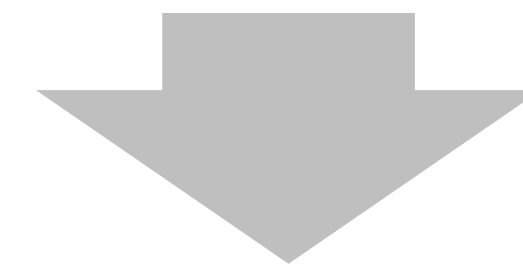


Hundreds of millions of  
compounds



Deep Neural  
Network

Novel compounds enhanced by bicarbonate



**NEXT GENERATION ANTIBACTERIAL DRUGS**



**MAYA FARHA, PHD**

**CEO**

- Research Associate, McMaster University
- Lead discoverer of the bicarbonate effect



**LINDSAY KALAN, PHD**

**RESEARCH LEAD, WOUND HEALING**

- Associate Professor, McMaster University; expertise in wound healing and infection
- Former Head of R&D with Exciton Technologies, Wound Care



**ERIC BROWN, PHD**

**CSO**

- Distinguished University Professor, McMaster University
- World-leading researcher (200 research papers) in antibiotic drug discovery



**JAKE MAGOLAN, PHD**

**RESEARCH LEAD, CHEMISTRY**

- Associate Professor, Department of Biochemistry, McMaster University
- Boris Family Chair in Drug Discovery



**GEORDIE STEWART, PHD, MBA**

**COO**

- Health, information and financial technology entrepreneur and executive
- Advisor to numerous startups and investors



**JONATHAN STOKES, PHD**

**RESEARCH LEAD, AI**

- Assistant Professor, Department of Biochemistry, McMaster University
- Research program in antibiotics using machine and deep learning

**ADVISORS**

**DAMIAN LAMB**

Genesys Capital Management Inc

**AMIE PHINNEY**

adMare BioInnovations

**GAY YUYITUNG**

McMaster Industry Liaison Office



If we don't change course, more than 10 million people will die annually from infection, more than currently die from all cancers.

(O'Neil Report on AMR, 2014)

**OUR MISSION IS TO PREVENT THIS FROM HAPPENING.**

## Connections/Partnerships...

**McMaster scientists**

**HHS clinicians**

**MILO**

**Gowlings**

## Funding...

**SOPHIE**

**McMaster Seed Fund**

What has the **Hamilton**  
Health Ecosystem done  
for us?

**Table 1. MIC<sub>50</sub> and MIC<sub>90</sub> Values for Azithromycin in the Absence and Presence of Bicarbonate against MRSA (n = 100), *S. pneumoniae* (n = 21), and *P. aeruginosa* (n = 92)**

|                                   | MRSA                      |                           | <i>S. pneumoniae</i>      |                           | <i>P. aeruginosa</i>      |                           |
|-----------------------------------|---------------------------|---------------------------|---------------------------|---------------------------|---------------------------|---------------------------|
|                                   | MIC <sub>50</sub> (µg/mL) | MIC <sub>90</sub> (µg/mL) | MIC <sub>50</sub> (µg/mL) | MIC <sub>90</sub> (µg/mL) | MIC <sub>50</sub> (µg/mL) | MIC <sub>90</sub> (µg/mL) |
| azithromycin                      | 128                       | >256                      | 16                        | >256                      | 64                        | 256                       |
| azithromycin + 25 mM bicarbonate  | 4                         | 4                         | 0.125                     | 4                         | 2                         | 4                         |
| azithromycin + 50 mM bicarbonate  | 1                         | 2                         | 0.0313                    | 0.25                      | 1                         | 2                         |
| azithromycin + 100 mM bicarbonate | 0.5                       | 1                         | 0.00319                   | 0.0625                    | 0.125                     | 1                         |

Bicarbonate enhances the **efficacy** and **spectrum** of many existing antibiotics, including Azithromycin

Azithromycin-bicarbonate is effective against key pathogens & drug-resistant bacteria. Pathogens tested (all susceptible):

- *Escherichia coli*
- *Burkholderia cenocepacia*
- *Acinetobacter baumannii*
- *Pseudomonas aeruginosa*
- *Enterococcus faecalis*
- *Klebsiella pneumonia*
- *Staphylococcus aureus*
- *Streptococcus pneumoniae*

-Farha, M. A *et al.*, Bicarbonate Alters Bacterial Susceptibility to Antibiotics by Targeting the Proton Motive Force. *ACS Infect Dis* 2018, 4 (3), 382-390.

-Farha, M. A *et al.*, Overcoming Acquired and Native Macrolide Resistance with Bicarbonate. *ACS Infect Dis* 2020, 6 (10), 2709-2718.

# Lung infections

Cystic Fibrosis presents a **unique** opportunity..

- **CFTR mutation: bicarbonate secretion is impaired**
  - Confirmed as the cause of aggregated/viscous mucus
- **Favorable effects with inhaled bicarbonate (ongoing trials)**
- **Safe and tolerable**
- **Increasing evidence that Azithromycin benefits CF patients**