

# World Leading Biopharma Company Seeking Strategic Collaborations for Phase III ready programs

## Hamlet Biopharma: Taking breakthrough science from discovery to clinic in areas of high unmet need.

### Translating Innovation Into Clinical Success: Three positive Phase II studies

Product Candidate	Indication	Discovery	Preclinical	Clinical	Phase II	Phase III
Alpha1H	Bladder Cancer	[Progress bar from Discovery to Phase II]				FDA Fast track
IL-1 receptor antagonist (anakinra)	Recurrent Urinary tract infection	[Progress bar from Discovery to Phase II]				
	Bladder Pain Syndrome	[Progress bar from Discovery to Phase II]				

- Strong clinical pipeline with advanced assets in bladder cancer, infection, and pain.
- Powerful discovery platform driving innovations in oncology and antibacterial treatments.
- Proven drug development expertise, offering valuable long-term partnership opportunities.

Successful Phase II studies in three clinical indications, driven by research originating from Hamlet's laboratories, with findings published in top journals like Nature.

1. **Bladder Cancer (Alpha1H)** – Placebo controlled study demonstrated significant tumor reduction in 88% of patients at higher doses. Striking induction of apoptosis, immune activation and down-regulation of cancer genes.
2. **Recurrent Urinary Tract Infections (Anakinra)** – Two arm study showed that anakinra was as effective as antibiotics, reducing symptoms and recurrence rates.
3. **Bladder Pain Syndrome (Anakinra)** – Treatment resulted in a significant reduction in pain and improved quality of life for patients with severe bladder pain.

### Alpha1H - Successful Phase II Completed in Bladder Cancer

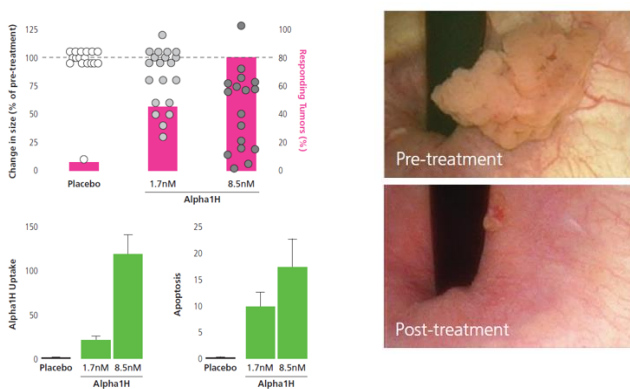
#### Alpha1H – Proven Clinical Anti-tumor Effect

- Dose-dependent efficacy, with 88% of patients treated with the higher dose experiencing partial or complete responses. Cancer specific effect. Healthy tissues do not take up the drug.
- Tumor cell **death by apoptosis** – striking difference between tumor and healthy tissue and low toxicity.
- Strong **immune activation** profile similar to BCG treatment.
- **Down-regulation of cancer genes** in the tumor – return towards a non-cancerous healthy profile.

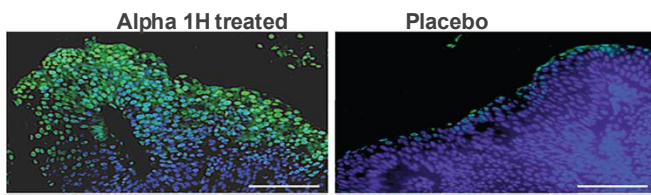
#### Commercial opportunity, bladder cancer

- ✓ Fast Track FDA designation with strong clinical data completed Phase 2.
- ✓ Positive FDA discussions ongoing for Phase III.
- ✓ GMP-ready for Phase III & commercialization.
- ✓ First-in-Class Neoadjuvant Non-Muscle Invasive Bladder Cancer Therapy.
- ✓ Strong IP positions with long lifetime.
- ✓ Manufacturing & CMC established.

#### Dose-Dependent Reduction in Tumor Number and Size after intra-vesical Alpha1H instillations



#### Increase in Alpha1H uptake and apoptosis in urine cells



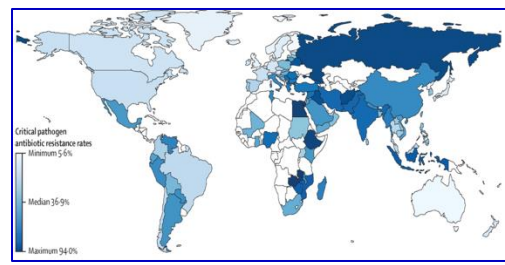
Increase in apoptosis in tumor tissues (in green) after Alpha1H instillation *Brisuda et al, Nature Communication, 2021*

### Hamlet Biopharma Objectives

- Complete Phase III trials and obtain market approval.
- Partner Late-Stage Assets – Secure partnerships for subsequent trials and global commercialization of Phase III-ready programs.
- Establish collaborations to advance preclinical assets.
- Grant access to early discovery programs through strategic collaborations.

## New Infection Treatment Paradigm: Immunotherapy as an Equally- Efficacious Alternative to Antibiotics

- Harnesses the immune response rather than directly targeting bacteria.
- Offers a proven, non-antibiotic approach for clearing antibiotic-resistant pathogens.



High antibiotic resistance rates for critical pathogens, world-wide

- Acute cystitis is a common infection of the urinary bladder, frequently caused by resistant bacteria
- **Phase II study – Blocking the IL1 receptor is as Effective as Antibiotics** – IL-1RA shows comparable outcomes to antibiotics in treating bacterial infections (recurrent cystitis)
- Evidence of effects against multi-resistant bacteria in animal models.
- **Breakthrough New Infection Treatment Paradigm** – Balances the immune response instead of killing bacteria with antibiotics.

### Outcome of two-armed Phase II study

- **Reduced symptoms**
- **Reduced recurrence rates**
- **improved quality of life**
- **Inhibition of immune hyperactivation**

### Advantages of acute immunotherapy

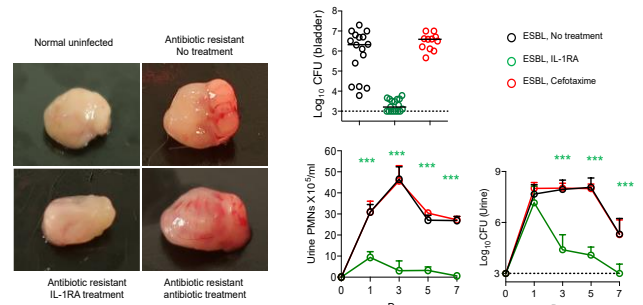
- Provides alternatives to antibiotics
- Reduces selective pressure on resistance
- Reduces effects on the normal flora in individual patients and in the population

## Extensive preclinical treatment effects in Acute Cystitis - IL-1RA

**IL-1RA – Treatment of acute cystitis in mice shows same Efficacy as Antibiotics** – IL-1RA shows comparable outcomes in cystitis and pyelonephritis/sepsis.

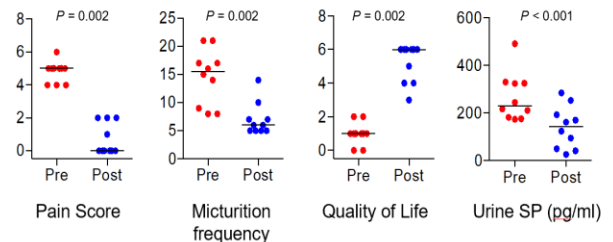
- **Potent Clearance of Antibiotic-Resistant Pathogens** – IL-1RA effectively eliminates resistant bacteria, demonstrating strong therapeutic potential.
- **Treatment efficacy against antibiotic sensitive** similar to cefalosporins. Clearance of cystitis and kidney infections after 7 days.
- **Treatment efficacy against antibiotic resistant strains** - IL-1RA shows similar efficacy on antibiotic-sensitive and antibiotic-resistant strains.

### Effect against resistant bacteria (ESBL)



## Successful Phase II completed in Bladder pain - IL-1RA

- **Bladder pain syndrome is a severe, debilitating disease of unknown origin.**
- Hamlet has shown that IL-1RA treatment significantly reduces pain and enhances the quality of life in severely disabled patients.
- **Direct Molecular Effects of IL-1RA on Pain sensing molecules** have been demonstrated in patients and experimental models.



## Intellectual Property and Preclinical Pipeline

- Hamlet owns 15 patent families including 8 families for cancer therapy.
- Issued patents and ongoing cases in USA, EU, Asia guarantee lasting protection and innovation potential.

For more information, please contact:

**PharmaVentures**  
the deal experts

**Adrian Dawkes,**  
Managing Director  
[adrian@pharmaventures.com](mailto:adrian@pharmaventures.com)

**Andreas Katsiamides,**  
Associate  
[andreas@pharmaventures.com](mailto:andreas@pharmaventures.com)



An innovative pharmaceutical company with a broad and strong portfolio of projects for the treatment of cancer and infections