Antitoxine™

(E)-N-(2,4-DINITROPHENOXY)-1-(4-FLUOROPHENYL)METHANIMINE

prepaire SHIELD

A TREATMENT AGAINST NERVOUS AGENTS

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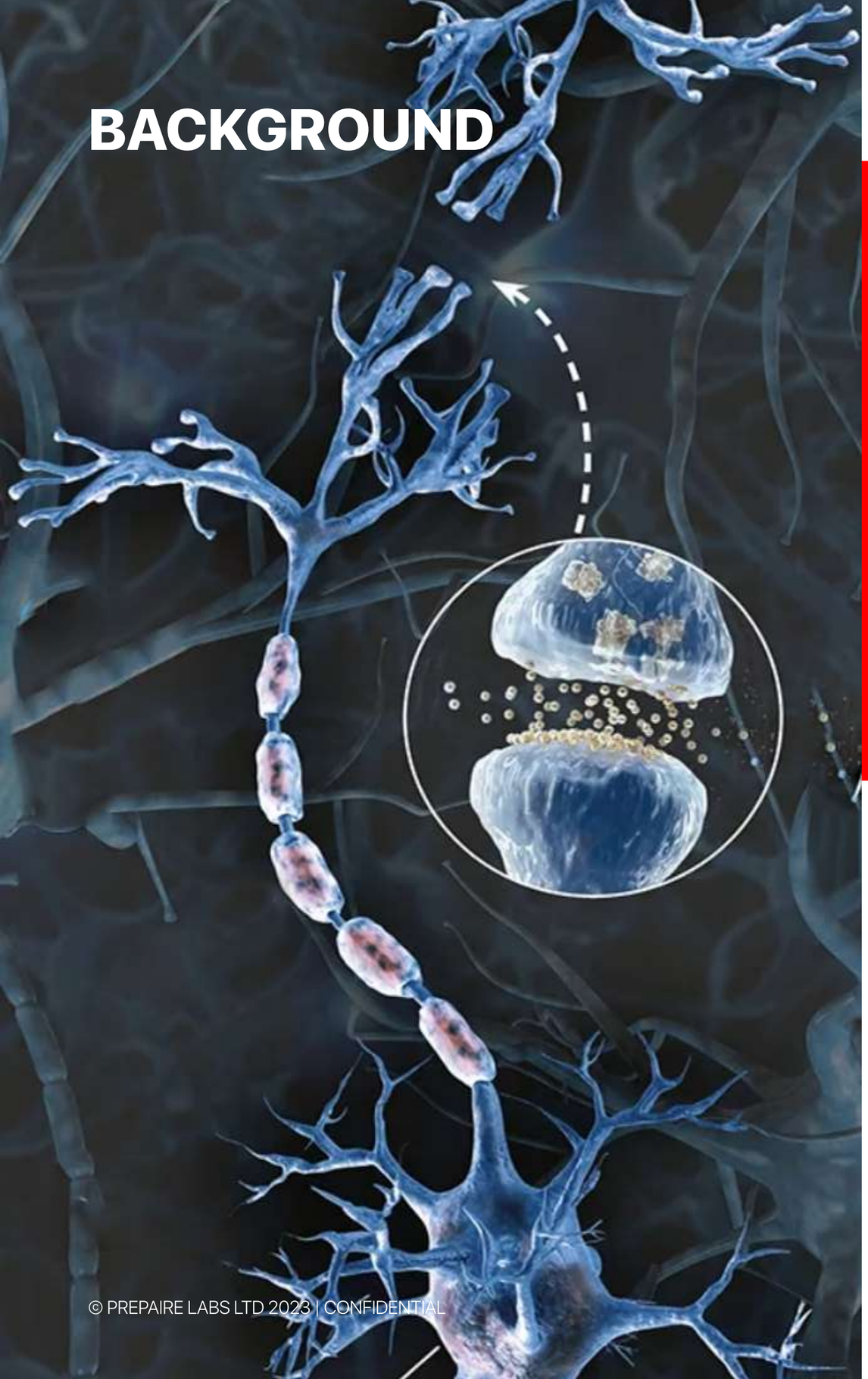
- Prepaire Shield integrates multi-level and multi-modal data (i.e. data ranging from the chemical level, pathways, and systems levels) through state-of-the-art AI-based solutions and provides a valuable opportunity to further understand the molecular mechanisms of CWA exposure in general, as well as patient phenotyping, assessment of patient trajectories as well as the clinical response to interventions at the onset of CWA exposure.

- In this context, Prepaire Shield goes beyond the traditional drug discovery process providing a fast, available and cost-effective platform for treatment design. Prepaire Shield integrates multi-modal/level data, a molecule design module, and a retrosynthesis tool to develop a comprehensive Clinical Decision Support system for measuring binding affinities between drugs and targets (including novel targets which may not have been discovered yet), assessing AChE reactivation with newly derived/synthesized oximes, and testing treatments with its comprehensive induced pluripotent stem cells (IPSCs) for management of patients exposed to CWAs.

- Following with this methodology we have developed a new oxime against nervous agents (organophosphores), which has been tested in-silico for efficacy and safety and is now ready for in-vitro assays.

- This system will empower caregivers in the use of novel management tools and combination therapies enabling the adoption of more effective management and personalized care by taking a systems-level approach to fine-tuning treatment and vital support.



BACKGROUND

- OP nerve agents (i.e., Sarin, Soman, or Tabun) are the most dangerous agents known, triggering seizure activity in the brain and leading to irreversible seizure-related brain damage.
- OP poisoning induces rapid death through different mechanisms, including respiratory and cardiovascular significant dysfunctions.
- OP nerve agents primarily act by inhibiting the enzyme acetylcholinesterase (AChE), causing an acute cholinergic crisis. Accordingly, medical countermeasures (MCMs) aim to minimize the cholinergic crisis upon deactivating AChE at the neuro synaptic and neuromuscular junctions or to remove the neurotoxic agent by some scavenging process.
- Despite the efforts to develop new oximes, the standard of care still relies upon a procedure dating from 1960 consisting of a combination of anti-cholinergic drugs (e.g. atropine), pralidoxime (2-PAM), obidoxime and benzodiazepines (e.g. diazepam).

- This protocol has remained in place despite the overwhelming scientific evidence that 2-PAM and obidoxime are generally regarded as the weakest AChE reactivators [1]. Moreover, 2-PAM is regarded as the most ineffective oxime from the perspective of treatment as well.
- In recent years (2006), asoxime chloride (HI-6) has been regarded as the gold-standard AChE reactivator [1] even though it has not yet been accepted as a common treatment due to the lack of field trials.

The new trends and development of neurologic IPSC organelles can expedite the clinical validation process whilst keeping the costs and risks under control throughout the whole validation process.

[1] Toxicol Rev 2006; 25 (4): 231-243

METHODOLOGY

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Treatment search

Virus/Bacteria
RNA/DNA

Target Disease
Protein

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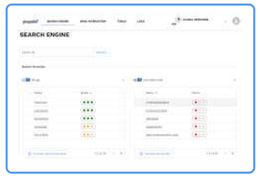
List of Molecules

TEM Proteins
Interaction
Binding



Selection of Molecule/s to test

Computational Trials

Large Population GENIE

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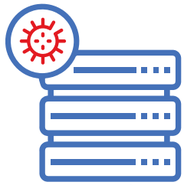
Repository Database



Feedback
Bias Correction / Update

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- APIs
- Machine Learning
- Artificial Intelligence
- Algorithms
- Protein unfolding
- Protein design

Target Drug Or Treatment Specifications

AutoMedic™

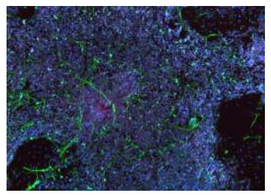
Researches Publications

NLP

Clinical Trials
Sentiment Analysis
End Points meta analysis

Patients Gene Samples

IPSC Fast production And delivery



In Vitro

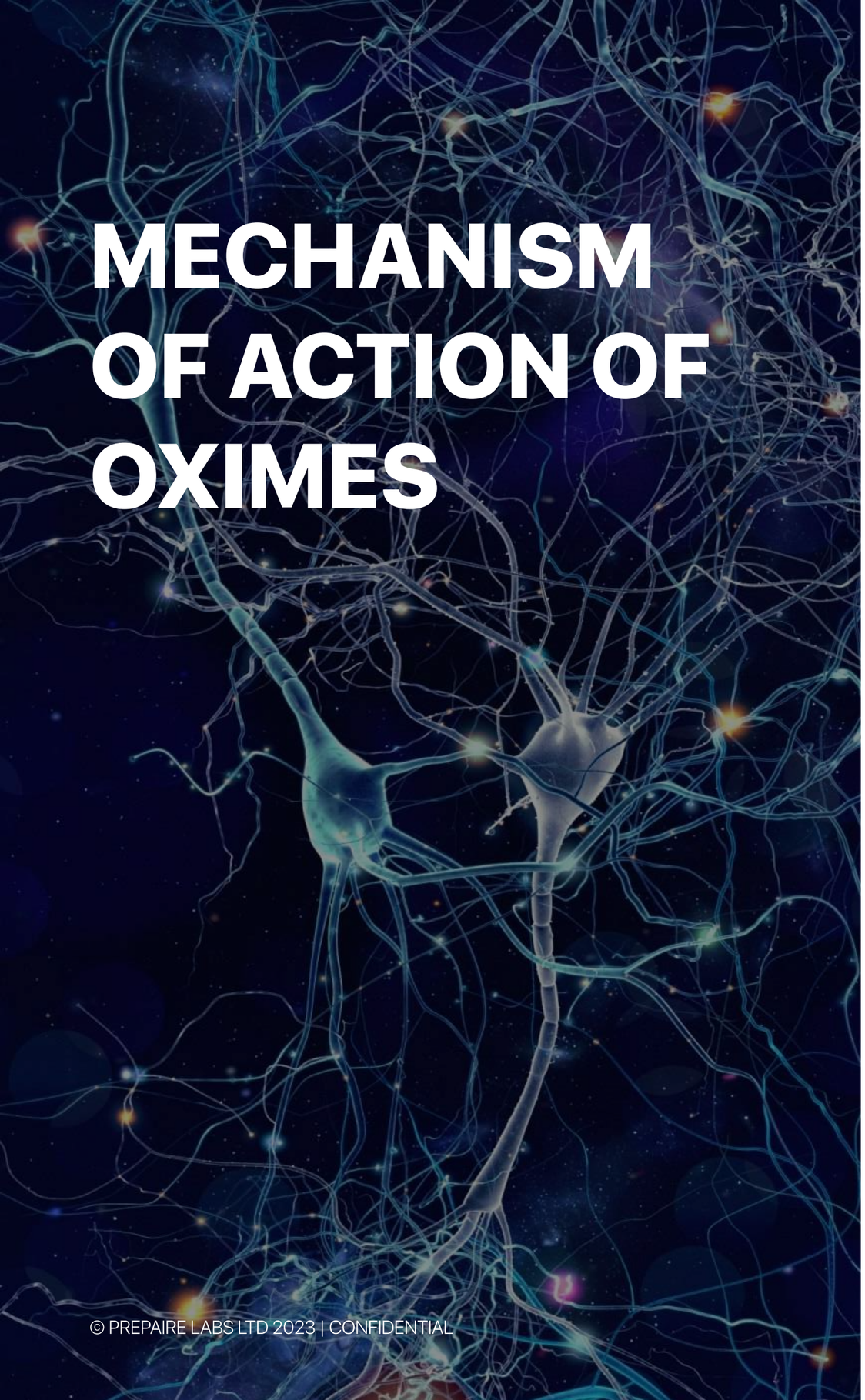
IN-SILICO Trials GENIE

FDA **Phase 1** FDA **Phase 2** FDA **Phase 3**

Clinical trials in-silico run in parallel with the normal trials to compare end-points, with the objective of gradually substitute normal ones

Approved Treatment

FDA



MECHANISM OF ACTION OF OXIMES

Organophosphates are chemicals that can cause poisoning by inhibiting an enzyme called acetylcholinesterase (AChE) in the nervous system. This leads to an accumulation of acetylcholine, a neurotransmitter, and overstimulation of the nervous system, leading to symptoms such as muscle twitching, convulsions, and respiratory failure.

Oximes in general (and the ones proposed here) work as an antidote for organophosphate poisoning by reactivating the inhibited acetylcholinesterase, thereby reducing the accumulation of acetylcholine and restoring normal nervous system function.

When an organophosphate molecule binds to acetylcholinesterase, it inactivates the enzyme and stops it from breaking down acetylcholine. Oximes are drugs that can help to reverse this inactivation by acting as a "bridge" between the acetylcholinesterase and the organophosphate molecule.

The oxime molecule attaches itself to both the acetylcholinesterase and the organophosphate molecule, helping to break the bond between them. This allows the acetylcholinesterase to regain its normal shape and function, so it can once again break down acetylcholine. This helps to reduce the amount of acetylcholine in the nervous system and relieve the symptoms of organophosphate poisoning.

In essence, the oxime acts as a sort of "intermediary" that helps to restore normal acetylcholinesterase function, thereby reducing the toxic effects of the organophosphate molecule.