A Strategic Plan for Securing Horizon Europe Funding and Commercializing a Novel Treatment for *Xylella fastidiosa*

Part I: The Strategic Context - Understanding the *Xylella fastidiosa* Challenge

1.1 The Pathogen: A Deep Dive into the Biology and Epidemiology of *Xylella fastidiosa* in Europe

Xylella fastidiosa represents one of the most significant and dangerous phytosanitary threats to European agriculture and ecosystems.[1] It is a gram-negative, slow-growing, and fastidious bacterium belonging to the Xanthomonadaceae family.[3] The pathogen's primary mode of action involves the colonization of the xylem vessels of host plants, the tissue responsible for transporting water and mineral nutrients from the roots to the leaves.[4] Once established, the bacteria multiply and form biofilms, which physically block the xylem network. This blockage leads to severe water stress and nutritional deficiencies, manifesting as characteristic disease symptoms such as leaf scorching, wilting, desiccation of branches, reduced fruit quality, declining yields, and ultimately, the death of the host plant.[2]

The threat posed by *Xylella fastidiosa* is amplified by its genetic diversity and broad host range. Globally, there are at least six recognized subspecies, of which four have been detected within the European Union: *fastidiosa*, *multiplex*, *pauca*, and *sandyi*.[4] These subspecies exhibit different levels of aggressiveness and preferences for different host plants, which complicates surveillance and control efforts. For instance, the devastating Olive Quick Decline Syndrome (OQDS) epidemic in Italy is associated with

Xylella fastidiosa subsp. *pauca*, while other outbreaks in Spain and France have

involved subsp. *fastidiosa* and *multiplex*.[2] This genetic variability underscores the need for robust solutions that can target the bacterium itself, rather than being tailored to a single strain or host.

The bacterium's host range is exceptionally wide and continues to expand. The European Food Safety Authority (EFSA) maintains a database that, as of mid-2024, lists over 700 plant species from 89 botanical families as potential hosts, with 452 species confirmed via the most stringent detection methods.[5] This list includes crops of immense economic importance to the EU, such as olive trees, grapevines, citrus, and stone fruits like almonds, plums, and cherries, as well as numerous ornamental and endemic wild plants.[1] A critical challenge is the existence of asymptomatic host species, which can act as silent reservoirs, facilitating the pathogen's spread to new areas and more susceptible crops without any visible signs of infection.[2]

Transmission of *Xylella fastidiosa* occurs via xylem sap-feeding insects. While various species of sharpshooters and froghoppers are vectors worldwide, the primary confirmed vector in Europe is the meadow spittlebug, *Philaenus spumarius*.[4] The widespread presence of this insect vector across the continent creates a high-risk pathway for the rapid dissemination of the pathogen.

Historically confined to the Americas, *Xylella fastidiosa* was first detected in the EU in 2013 in the Apulia region of Southern Italy.[3] This event marked a major shift in the pathogen's known geographical distribution. Since then, official surveys have confirmed its establishment in demarcated areas of France (Corsica and PACA), Spain (Balearic Islands, Madrid, Valencia), and Portugal.[3] The pathogen's spread is believed to have been facilitated by the global trade of infected plant materials.[4] Furthermore, climate change models predict that rising global temperatures could expand the pathogen's viable range further north in Europe, beyond the Mediterranean basin, with a 3°C temperature increase identified as a potential tipping point for a dramatic expansion.[4] This combination of a highly adaptable pathogen, a vast host range, an efficient vector, and favorable climatic trends creates an urgent and escalating threat to the entire European Union.

1.2 The Devastation: Quantifying the Economic, Agricultural, and Social Impact Across the EU

The economic and social consequences of a full-scale *Xylella fastidiosa* invasion in

Europe would be catastrophic. The European Commission has estimated that, in a scenario of full spread, the bacterium could cause annual production losses of **€5.5 billion**.[1] This figure represents a direct threat to the agricultural heartlands of the Mediterranean and beyond, putting at risk nearly

300,000 jobs directly involved in the production of susceptible crops.[1]

The impact is not distributed evenly but threatens the very foundation of key agricultural sectors. The analysis projects that the disease could affect:

- **70% of the EU production value of older olive trees** (over 30 years old) and 35% of younger ones.
- **13% of the EU production value of almonds**.
- **11% of the EU production value of citrus**.
- **1-2% of the EU production value of grapes**.[1]

The situation in Apulia, Italy, serves as a stark and tangible case study of this potential devastation. Since the first outbreak in 2013, the OQDS epidemic has led to the death and uprooting of millions of olive trees, many of which were centuries-old and formed an irreplaceable part of the region's landscape and heritage.[3] In this region, olive production has collapsed by an alarming 65-80%, leading to the loss of an estimated 100,000 jobs on farms and in the associated supply sector.[9] Economic models for Italy alone project a potential impact over 50 years ranging from €1.9 billion to €5.2 billion if production ceases after orchards die off.[2]

Beyond the direct economic losses, the impact of *Xylella fastidiosa* extends into the social and cultural fabric of affected communities. The mandatory control measures, particularly the felling of infected and surrounding trees, have caused significant societal unrest and political friction, pitting regulatory necessity against the deep cultural and economic attachment of farmers to their land and crops.[2] The destruction of ancient olive groves, which have been cultivated for generations, represents an irreversible loss of cultural and natural heritage, fundamentally altering landscapes and threatening a way of life that has defined Mediterranean communities for centuries.[3] The disease thus poses not merely an agricultural problem but a profound crisis for the economic stability, social cohesion, and cultural identity of vast regions within the European Union.

1.3 The Stalemate: Analysis of Current Control Strategies and Their Inadequacy

In response to the escalating threat, the EU has classified *Xylella fastidiosa* as a priority quarantine pest and has implemented a stringent regulatory framework to prevent its introduction and spread.[4] The core of the EU's strategy is governed by regulations such as Commission Implementing Regulation (EU) 2020/1201, which mandates a defensive posture focused on containment and eradication, as there is currently

no known curative treatment for infected plants.[4]

This strategy relies on a set of phytosanitary measures, including:

- **Establishment of Demarcated Areas:** Upon detection of the pathogen, Member States must establish an "infected zone" around the positive plant(s) and a surrounding "buffer zone." The width of these zones can range from a 50-meter radius around an infected plant to a buffer zone of up to 5 kilometers, depending on the outbreak's context.[1]
- **Eradication and Plant Removal:** Within these zones, there is a requirement for the immediate removal and destruction of all infected plants. In some cases, regulations have mandated the removal of all potential host plants within a specified radius (e.g., 100 meters) of an infected plant, regardless of their health status, though this has been modified in some regions to mitigate wiping out entire agricultural landscapes.[11]
- **Vector Control:** Management strategies focus heavily on reducing the population of the insect vector, *Philaenus spumarius*. This is achieved through agricultural practices like soil tillage (which can reduce vector populations by up to 60% by destroying eggs and nymphs) and the subsidized use of authorized insecticides such as Kaolin, Deltamethrin, and Lambda-Cyhalothrin.[4]
- **Movement Restrictions:** Strict controls are placed on the movement of specified plants for planting out of demarcated areas to prevent human-assisted spread.[11]

While these measures are essential for slowing the pathogen's advance, they are fundamentally reactive and come with significant drawbacks. They are economically costly, environmentally impactful (due to increased insecticide use), and socially divisive.[2] The success of eradication efforts depends heavily on early detection and the full cooperation of farmers and local authorities, which is not always achievable.[11]

The European Union has invested significantly in research through its framework programmes, including Horizon 2020 and Horizon Europe.[4] Major projects like

POnTE (Pest Organisms Threatening Europe) and **XF-ACTORS** (Xylella Fastidiosa Active Containment Through a multidisciplinary Oriented Research Strategy) have made crucial contributions to understanding the pathogen's biology, genetics, epidemiology, and vector interactions, as well as developing better detection and risk assessment models.[1] More recent projects like

BIOVEXO are exploring novel biopesticides, aiming to bring solutions to a high Technology Readiness Level (TRL 7-8) by 2025.[1]

However, an analysis of this entire strategic landscape—from regulatory actions to the research portfolio—reveals a consistent and critical gap. The entire European strategy is a holding action, predicated on the stark reality that there is no cure. The focus has been on containment, detection, and management in the absence of an effective therapeutic tool. This defensive posture, born of necessity, highlights a profound innovation vacuum. A project that proposes a credible pathway toward a curative or a highly effective, systemic preventative treatment would not be an incremental improvement; it would fundamentally disrupt the current paradigm and address the single greatest failure point in the EU's fight against *Xylella fastidiosa*.

Part II: The Innovation Gap and Your Competitive Edge

2.1 The Scientific Frontier: A Review of Emerging Research on *Xylella* Treatments

While a definitive cure for *Xylella fastidiosa* remains elusive, the global scientific community is actively exploring several promising avenues for disease mitigation and control. A thorough understanding of this research landscape is essential to position a novel chemical approach as a distinct and high-impact alternative. Current efforts can be broadly categorized into biological controls, plant-based resistance strategies, and the application of natural compounds.

Biological Control (Biocontrol): This approach seeks to use living organisms or their by-products to suppress the pathogen or its vector. Key strategies include:

- **Antagonistic Endophytes:** Researchers are investigating endophytic

microorganisms—microbes that live within plant tissues without causing harm—that can outcompete or inhibit *Xylella*. For example, the grapevine endophyte *Paraburkholderia phytofirmans* PSjN has been shown to reduce disease symptoms, and can even be applied as a foliar spray. However, its effectiveness is limited by the durability of its colonization in the host plant, particularly in olives.[17]

- **Non-Virulent Strains:** An early biocontrol strategy involved inoculating grapevines with weakly virulent strains of *Xylella fastidiosa* isolated from other hosts. This was believed to induce a protective immune response in the plant, offering protection from more severe disease for several years.[17]
- **Vector Biocontrol:** Efforts are also directed at the insect vector. One study proposed the inundative release of *Zelus renardii*, a natural predator of the spittlebug *Philaenus spumarius*, as a "green" alternative to chemical insecticides. Simulations suggested this could reduce pathogen incidence significantly, but it requires in-field validation and large-scale rearing of the predator.[18]
- **Biopesticides:** The ongoing BIOVEXO project is a major EU initiative focused on testing six innovative biocontrol solutions, including bacterial strains, a microbial metabolite, plant extracts, and an entomopathogenic fungus, targeting both the bacterium and its vector.[9]

Plant Resistance and Defense Priming: This line of research focuses on the host plant's own capabilities.

- **Breeding for Resistance:** A long-term and crucial strategy is the identification and breeding of resistant plant cultivars. For example, the devastating impact on Italian olive groves has spurred research into identifying olive varieties with higher tolerance or resistance to the pathogen.[2]
- **Immune System Priming:** Research has shown that plants can mount an immune response against *Xylella*. One approach involves "priming" this defense system by exposing the plant to bacterial components, such as lipopolysaccharide (LPS), a molecule from the bacterium's outer membrane. Pre-exposure to LPS has been shown to reduce disease symptoms in grapevine.[17]

Natural Compounds and Sustainable Treatments: This avenue explores the antimicrobial properties of naturally occurring molecules.

- **Phenolic Compounds:** Various plant-derived phenolic compounds, including catechol, caffeic acid, and resveratrol, have demonstrated inhibitory activity against *Xylella fastidiosa* in *in vitro* assays.[20] Other studies have shown that compounds like epicatechin and gallic acid can reduce the bacterium's ability to adhere to surfaces and form aggregates, which are crucial steps in biofilm

formation.[20]

- **Other Approaches:** Other experimental strategies include "cold therapy," which exploits the bacterium's sensitivity to low temperatures, and the application of various minerals and compounds, though their large-scale use has often been deemed economically expensive.[11]

While these approaches are valuable and form part of a necessary integrated pest management (IPM) strategy, they each face significant hurdles to widespread, effective deployment. Biological controls can be difficult to scale, may have limited efficacy across different environments and hosts, and face their own regulatory pathways. Breeding for resistance is a slow, generational process. Natural compounds often show promise *in vitro* but may lack the stability, systemic mobility, or potency required for effective field application. This context reveals a clear and persistent gap for a solution that is potent, scalable, stable, and systemically active within the plant—characteristics that are the hallmark of a well-designed synthetic chemical treatment.

2.2 A Novel Chemical Approach: The Scientific Rationale for Phosphinic Acid Derivatives Against a Gram-Negative Bacterium

The proposed project pivots away from the prevailing biological and breeding-focused research avenues to introduce a novel, targeted chemical strategy. This approach is grounded in established biochemical principles but applies them in an innovative context, directly addressing the "no cure" reality of the *Xylella fastidiosa* crisis. The scientific rationale rests on a strategic "jump" from the known fungicidal properties of phosphonic acids to the potential bactericidal properties of novel phosphinic acid derivatives against a gram-negative bacterium.

First, it is crucial to acknowledge the existing use of a related class of compounds in agriculture. Phosphonic acids, commonly known as phosphonates, have been used for decades as effective systemic fungicides, particularly against oomycete pathogens like *Phytophthora* and *Pythium*.[22] Their mode of action is understood to be twofold: they have a direct inhibitory effect on the pathogen's metabolism and they stimulate the plant's own natural defense systems.[23] However, their primary application has been against fungus-like organisms, not bacteria.

The critical scientific precedent that makes this project viable is the established

antibacterial activity of a specific phosphonate compound: **Fosfomycin**. *Xylella fastidiosa* is a gram-negative bacterium.[3] Fosfomycin is a broad-spectrum phosphonate antibiotic that is clinically effective against a wide range of both gram-positive and gram-negative bacteria.[28] Its mechanism is well-understood: it is a structural mimic of phosphoenolpyruvate (PEP) and acts by irreversibly inhibiting the enzyme MurA, which catalyzes the first committed step in the biosynthesis of the bacterial cell wall (peptidoglycan).[30] Because it targets a fundamental and highly conserved bacterial process, it has broad efficacy.

This precedent provides the foundation for the project's central research hypothesis: **If a phosphonate (Fosfomycin) can be a potent antibiotic, then it is plausible that other, novel organophosphorus compounds, specifically phosphinic acid derivatives, can be designed to act as targeted, systemic bactericides against *Xylella fastidiosa*.**

Phosphonates and phosphinates are powerful enzyme inhibitors because they are stable isosteres (mimics) of labile natural substrates like phosphate esters or carboxylates.[30] They can bind to the active site of an enzyme but, due to their highly stable carbon-phosphorus (C-P) bond, they cannot be processed, thus blocking the enzyme's function.[31] The project's core activity will be to leverage this principle by designing and synthesizing a library of novel phosphinic acid derivatives. The research will aim to identify compounds that can:

1. Be readily absorbed and translocated systemically throughout the plant's xylem and phloem, a known property of phosphonates that makes them ideal for treating xylem-limited pathogens.[22]
2. Target essential and ideally unique metabolic pathways within *Xylella fastidiosa*, minimizing off-target effects on the host plant or beneficial microorganisms.
3. Potentially induce a host defense response, providing a dual-action mechanism of control similar to that observed with phosphonate fungicides.[26]

This approach is not an incremental improvement of an existing technology but a paradigm shift. It moves beyond the limitations of conventional insecticides that only target the vector and proposes a direct, therapeutic intervention against the pathogen within the plant. It offers the potential for a solution that is more scalable and faster to deploy than breeding programs and potentially more potent and stable than many biological or natural-compound-based approaches.

2.3 Leveraging Your Assets: Positioning Your Brother's PhD and Expertise as a

Unique Selling Proposition

A critical component of any successful Horizon Europe proposal, particularly under the "Excellence" criterion, is the demonstrated capacity of the consortium to achieve the project's ambitious objectives. In this context, the specific and specialized expertise of the core team is a paramount asset. The project's scientific leadership possesses a doctoral degree with a thesis on "Contributions to the Chemistry and applications of phosphinic acids" [User Query]. This qualification is not merely a general background in chemistry; it represents a unique and powerful competitive advantage that must be strategically positioned at the forefront of the proposal narrative.

This niche expertise transforms the project from a speculative exploration into a focused, expert-led endeavor. The proposal will not suggest a broad, unfocused screening of random compounds. Instead, it will articulate a strategy based on rational drug design, guided by deep, documented knowledge of phosphinic acid chemistry. This specific expertise allows the project to claim several key advantages:

- **Novelty and Innovation:** The project is not limited to testing existing, commercially available phosphonates. The team's core competency lies in the synthesis of **novel phosphinic acid derivatives**. This is a crucial distinction. Phosphinic acids (R2P(O)OH) offer different structural and electronic properties compared to phosphonic acids (RP(O)(OH)2), providing a vast and underexplored chemical space for identifying potent bactericides. The proposal can credibly claim to be pioneering a new class of chemical agents for this specific application.
- **Scientific Credibility:** The PhD credential provides tangible proof of world-class expertise in the exact chemical family being investigated. This immediately answers any questions an evaluator might have about the team's ability to execute the complex chemical synthesis and characterization required in the early work packages. It demonstrates that the project is built on a foundation of years of specialized academic research.
- **De-risking the Research Plan:** The proposal can argue that the team's prior experience significantly de-risks the most innovative part of the project—the creation of the compound library. The team already possesses the know-how for synthesis, purification, and analysis of these specific molecules, allowing the project to proceed more efficiently and with a higher probability of success.

In the proposal, this asset should be highlighted in the description of the core team

and linked directly to the objectives of the work packages focused on chemical synthesis (e.g., WP2 in the proposed structure). The narrative should emphasize that the project's scientific lead is a recognized expert in the field, ensuring that the exploration of this novel chemical space is not a random walk but a guided, intelligent search for a solution. This transforms a personal qualification into a strategic asset that underpins the entire project's claim to excellence and feasibility.

Part III: Navigating the Horizon Europe Funding Landscape

3.1 An Overview of Horizon Europe: Understanding the Structure, Pillars, and Strategic Priorities

Successfully securing funding from Horizon Europe requires more than a scientifically brilliant idea; it demands a sophisticated understanding of the programme's structure, objectives, and underlying political priorities. Horizon Europe is the EU's flagship funding programme for research and innovation for the 2021-2027 period, with an indicative budget of €93.5 billion.[33] Its structure is organized into three main pillars, with a fourth component focused on widening participation.

For a project of this nature, the most relevant component is **Pillar II: Global Challenges and European Industrial Competitiveness**.[33] This pillar is designed to tackle major societal challenges and to reinforce technological and industrial capacities. It is implemented through six thematic "Clusters," each addressing a different area of global concern.

The proposed project aligns perfectly with **Cluster 6: Food, Bioeconomy, Natural Resources, Agriculture and Environment**. This cluster, with a budget of approximately €9 billion for 2021-2027, is the primary vehicle through which the EU funds research and innovation to create sustainable, healthy, and inclusive food systems and to protect the environment.[34]

Crucially, a competitive proposal must demonstrate strong alignment with the EU's highest-level policy objectives. This project directly supports several key initiatives:

- **The European Green Deal:** This is the EU's overarching strategy for creating a modern, resource-efficient, and competitive economy with no net emissions of greenhouse gases by 2050. A project that provides a sustainable solution to a devastating plant disease, thereby protecting agricultural productivity and reducing reliance on broad-spectrum insecticides, is a direct contribution to the Green Deal's goals.[36]
- **The Farm to Fork (F2F) Strategy:** As a cornerstone of the Green Deal, the F2F strategy aims to make food systems fair, healthy, and environmentally-friendly. It explicitly calls for a reduction in the reliance on pesticides and the promotion of Integrated Pest Management (IPM). Developing a novel, targeted plant protection product is precisely the kind of innovation the F2F strategy seeks to foster.[34]
- **EU Competitiveness and Strategic Autonomy:** The threat of *Xylella fastidiosa* is not just environmental but also economic, jeopardizing a multi-billion-euro industry and Europe's food sovereignty in key products like olive oil and almonds.[1] A successful project would bolster the competitiveness and resilience of the European agri-food sector, a core priority for the EU.[42]

By framing the project within this strategic policy context, the proposal moves beyond a purely scientific exercise and presents itself as a vital tool for achieving the EU's most pressing political and economic goals. This demonstrates to evaluators a mature understanding of why the EU funds such research and positions the project as a high-impact investment for the European taxpayer.

3.2 Pinpointing the Opportunity: In-Depth Analysis of Call HORIZON-CL6-2025-02-FARM2FORK-01-two-stage

Within the vast landscape of Horizon Europe, identifying the single most appropriate funding call is a critical strategic decision. Based on a thorough analysis of the 2025 Work Programmes, the ideal target for this project is unequivocally **HORIZON-CL6-2025-02-FARM2FORK-01-two-stage: Emerging and future risks to plant health**.[44] This call is not merely a good fit; its structure and objectives appear tailor-made for a high-risk, high-reward project led by a new and innovative team.

Dissection of the Call's Scope and Expected Outcomes:

The call title itself, "Emerging and future risks to plant health," signals an interest in novel threats and, by extension, novel solutions beyond incremental improvements.

The expected outcomes of projects funded under this topic align perfectly with the proposed research [46]:

1. **Deeper insight into biological and socio-economic drivers of pest emergence:** The project will provide fundamental insights into the chemical vulnerabilities of *Xylella fastidiosa*, a key biological aspect driving its impact.
2. **Cost-effective prevention and control tools consistent with Integrated Pest Management (IPM):** The ultimate goal is to develop a novel chemical compound that can be formulated into a cost-effective product, becoming a new and essential tool within IPM strategies for olive, almond, and other affected crops.
3. **Economic, social, and environmentally sound solutions for effective pest management:** By aiming for a highly targeted bactericide, the project seeks a solution with a better environmental profile than broad-spectrum insecticides. Its success would have profound positive economic and social impacts on affected rural communities.
4. **Scientific support, recommendations, and policy advice to strengthen plant health policies:** The project's results, particularly the validation of a new class of active substance against a priority quarantine pest, would provide critical scientific evidence to inform and strengthen future EU plant health regulations.

Analysis of Key Call Characteristics:

The administrative and strategic features of this call are particularly advantageous for this project:

- **Type of Action: Research and Innovation Action (RIA).** This confirms that the primary focus is on research and development activities—from fundamental research to testing and validation in a lab and relevant environment. This is perfectly suited for a project aiming to move from a chemical concept (TRL 2-3) to a field-tested prototype (TRL 5-6).[48]
- **Indicative Budget:** The call has a total indicative budget of €12 million, with an expected EU contribution of around **€6 million per project**.[49] This substantial budget allows for the formation of a robust, multi-partner consortium and the execution of an ambitious, multi-year research plan that includes chemical synthesis, extensive trials, and dissemination activities.
- **Two-Stage Submission Process:** This is a significant strategic advantage. The first stage requires only a concise, 10-page proposal. This reduces the initial administrative burden and allows the team to focus on articulating the core concept's excellence and impact. Only if the project passes this first hurdle is a full proposal required.[51]
- **Blind Evaluation Pilot:** The first stage of this call is part of a "blind evaluation"

pilot. Applicants must not disclose their names or institutions in the proposal. This is a deliberate mechanism by the European Commission to level the playing field. It forces evaluators to judge the proposal based solely on the scientific merit, novelty, and potential impact of the idea, removing any potential bias towards large, well-known universities or research institutions. For a new SME-led consortium, this is an invaluable opportunity to compete on the quality of the idea alone.[46]

- **Lump-Sum Funding:** The call utilizes a lump-sum funding model. This means payments are tied to the successful completion of work packages, not the meticulous reporting of individual costs (e.g., timesheets, receipts). This dramatically simplifies financial administration and reduces the bureaucratic overhead for the coordinator, which is a major benefit for an SME.[48]
- **Timeline:** The deadlines are clearly defined: **04 September 2025** for the Stage 1 proposal and **18 February 2026** for the Stage 2 proposal for successful applicants.[51] This provides a concrete timeline for planning, consortium building, and proposal writing.

The combination of these features—a thematically perfect scope, a substantial budget, and a submission process designed to favor innovative ideas over institutional prestige—makes HORIZON-CL6-2025-02-FARM2FORK-01-two-stage the optimal strategic target.

Table 3.1: Comparative Analysis of Relevant Horizon Europe Funding Calls

Call Identifier	Call Title	Type of Action	Indicative Budget/Project	Scope and Rationale for Selection/Rejection
HORIZON-CL6-2025-02-FARM2FORK-01-two-stage	**Emerging and future risks to plant health**	**RIA**	**~€6 million**	**Primary Target.** The scope is a perfect match, focusing on novel solutions for major plant health threats. The RIA format, two-stage blind evaluation, and lump-sum funding are

				strategically ideal for an innovative, SME-led project.[45]
HORIZON-CL6-2025-01-BIODIV-02-two-stage	Breeding for resilience: enhancing multi-stress tolerance in crops	RIA	~€7 million	**Poor Fit.** This call focuses exclusively on plant breeding and genetic approaches to achieve resilience. It does not accommodate proposals for chemical control solutions.[37]
HORIZON-EIC-2025-PATHFINDERCHALLENGES-01-01	Biotech for Climate Resilient Crops and Plant-Based Biomanufacturing	EIC Grants (RIA)	Not Specified	**Poor Fit.** While related, EIC Pathfinder Challenges are for much earlier-stage, radical science (typically TRL 1-3) and this specific call is focused on biotechnology, not synthetic chemistry. The proposed project is more applied than a typical Pathfinder project.[52]
BIOVEXO Project (H2020)	Biocontrol of Xylella and its vector in olive trees for integrated pest	IA	~€7 million (Total)	**Comparison/Justification.** This completed project serves as a useful

	management			benchmark. Its focus was on biopesticides (bacterial strains, fungi, plant extracts). The proposed project is clearly differentiated by its focus on novel synthetic chemistry, addressing a gap not covered by BIOVEXO.[10]

Part IV: A Blueprint for a Winning Proposal

4.1 The Consortium: Architecting a Balanced, Multi-Actor Partnership

Crafting a compelling Horizon Europe proposal begins with assembling a world-class consortium. The composition of the partnership is not merely an administrative formality; it is a direct reflection of the project's credibility and its ability to deliver on its promises. For a call under Cluster 6, the consortium must be structured not only to meet the formal eligibility criteria but also to embody the "Multi-Actor Approach" (MAA), a philosophy central to ensuring that research outcomes are practical, relevant, and readily adopted.[53]

Formal Eligibility and the Multi-Actor Approach (MAA):

The baseline eligibility requirement for a standard collaborative project is a consortium of **at least three independent legal entities, each established in a different EU Member State or Associated Country**, with at least one of these being from an EU Member State.[48]

However, the MAA demands a more sophisticated structure. It requires the active and

continuous involvement of a diverse range of actors throughout the project's lifecycle, from co-designing the research questions to participating in experiments and disseminating the results. For this project, a well-balanced, multi-actor consortium should include:

- **Research & Technology Organisations (RTOs)/Universities:** To provide fundamental scientific expertise in plant pathology, microbiology, and agronomy. They will be crucial for conducting *in vitro*, laboratory, and greenhouse trials.
- **End-Users (Farmers, Agricultural Cooperatives):** To ensure the project remains grounded in real-world needs. They will provide test sites ("Living Labs") for field trials, offer practical feedback on potential product formulations and application methods, and act as powerful ambassadors for the project's results within the farming community.
- **Industry Partners (SMEs or Large Enterprises):** To bring in commercial and industrial expertise. This could include a company specializing in the formulation of agrochemicals, which would be vital for turning a synthesized active ingredient into a stable, sprayable product. Another industry partner could be from the agrochemical distribution sector, providing insights into market access and regulatory pathways.
- **Advisory/Extension Services or Policy-Advising Bodies:** To bridge the gap between research and practice/policy. Their involvement ensures that the project's outputs are translated into practical advice for farmers and robust data for policymakers, directly addressing the call's objective to support plant health policy.[47]

The SME as Coordinator: A Strategic Hybrid Model:

The decision of who coordinates the project is critical. While it is common for large universities to take the lead, an SME coordinator signals strong commercial ambition and a clear exploitation path, which is highly valued by the European Commission. However, the administrative and financial responsibilities can be daunting for a small organization.[55]

A highly effective and de-risked strategy is the **Hybrid Coordinator Model**.

1. **Your Startup as Official Coordinator and Scientific Lead:** Your newly formed SME will be the legal entity named as the Coordinator in the Grant Agreement. This gives you ultimate control over the project's direction, budget allocation, and intellectual property strategy. You and your brother will be the scientific and managerial driving force, a role you are best placed to fill.[57]
2. **Delegation of Administrative Tasks:** The Horizon Europe Grant Agreement

explicitly allows the coordinator to delegate certain administrative and financial management tasks to another beneficiary.[55] Your consortium should therefore include a partner—ideally a university or RTO with a professional and experienced EU projects office—that will be contractually assigned (via the Consortium Agreement) the responsibility for managing financial reporting, collecting deliverables, and handling communication with the Commission's project officer.

This hybrid structure presents the evaluators with the best of both worlds: the clear commercial drive and scientific leadership of an SME, combined with the proven administrative stability of an experienced academic institution. This robust management structure will score highly under the "Implementation" criterion in the Stage 2 evaluation.

Partner Search Strategy:

Identifying the right partners is an active process. The following resources should be utilized:

- **EU Funding & Tenders Portal:** The official portal has a partner search function where organizations can post their expertise and interest in specific calls.[54]
- **National Contact Points (NCPs):** Each country has NCPs for Horizon Europe who can provide support and help with partner searches through their networks.[54]
- **Brokerage Events:** The European Commission and NCP networks often organize brokerage events (online or in-person) specifically for upcoming calls, where you can pitch your idea and meet potential partners.[51]
- **Partner Search Platforms:** Platforms like the one hosted by b2match for the CARE4BIO NCP network show active searches from organizations looking to join or build consortia for this specific call, providing direct leads.[58]

Table 4.1: Template for Consortium Partner Roles and Expertise Matrix

Partner Type	Partner Name (TBD)	Country (Example)	Key Project Role(s)	Justification of Expertise and Contribution
SME (Coordinator)	*Your Startup*	*Your Country*	**Coordinator; Scientific Lead (WP2); Exploitation Lead (WP6)**	Doctoral-level expertise in phosphinic acid chemistry. Will lead the design

				and synthesis of novel compounds and drive the commercializati on strategy.
University	University of Valencia (UPV)	Spain	**Administrative Support Lead; Lead of Lab/Greenhous e Trials (WP3, WP4)**	Extensive experience managing EU projects. Leading research group in plant pathology with specific expertise in *Xylella* and containment facilities for testing.
Research Org.	National Research Council (CNR)	Italy	**Lead of Field Trials (WP5)**	World-renowne d expertise from the Apulian outbreak. Access to infected olive groves for "Living Lab" field trials. Strong connections to local growers.
Farmer's Cooperative	*Coop Name*	Portugal	**End-User Partner; Field Trial Site (Almonds)**	Represents hundreds of almond growers. Will co-design trial protocols for practical relevance, host field trials, and lead farmer-to-farme

				r dissemination.
Industrial SME	*Formulation Company*	Germany	**Industrial Partner; Formulation & Scalability Advisor (WP6)**	Specializes in the formulation of plant protection products. Will advise on developing the active ingredient into a stable, effective, and commercially viable product.
Advisory Body	*Regional Plant Health Service*	France	**Advisory Board Member; Dissemination Partner (WP6)**	Provides a direct link to national plant health authorities and extension services. Will help translate results into policy briefs and practical guidelines for inspectors and advisors.

4.2 The Proposal (Stage 1 - Blind Evaluation): Mastering the 10-Page Submission

The Stage 1 proposal is a high-stakes, 10-page document that will be judged entirely on its anonymous content. With the evaluators blinded to the applicants' identities, the proposal must succeed on the sheer force of its idea.[49] The evaluation at this stage is focused exclusively on two criteria:

Excellence and **Impact**.[46] The structure should be clear, concise, and compelling, telling a powerful story that captures the evaluator's attention.

Section 1: Excellence (Approx. 5 pages)

This section must establish the project's scientific and technological ambition, novelty, and soundness.

- **Objectives and Ambition:** Begin with a bold and clear statement of the project's overall objective: "To design, synthesize, and validate a new class of systemic, curative phosphinic acid-based bactericides specifically targeting *Xylella fastidiosa*, providing the first effective therapeutic solution to the European agricultural crisis it has caused." This immediately frames the project as ambitious and solution-oriented.
- **Relation to the State-of-the-Art:** Briefly summarize the current stalemate (containment, no cure) and the limitations of existing research avenues (biocontrol, breeding), as detailed in Part II. This demonstrates awareness of the current landscape.
- **Novelty and Methodology:** This is the core of the Excellence section.
  - Introduce the novel concept: the strategic pivot from known phosphonate fungicides to novel phosphinic acid bactericides.
  - Explain the scientific rationale: cite the precedent of Fosfomycin's efficacy against gram-negative bacteria and its mechanism of action (inhibiting MurA).[30]
  - Describe the proposed methodology in a logical flow:
    1. *Rational Design:* Use computational modeling and structural biology to identify potential enzyme targets within *Xylella fastidiosa*'s metabolism.
    2. *Synthesis:* Create a focused library of novel phosphinic acid derivatives designed to mimic the natural substrates of these target enzymes.
    3. *Screening:* Detail the multi-step screening process, starting with *in vitro* assays for bactericidal/bacteriostatic activity, followed by lab-based tests on infected plant tissues.
  - Emphasize the interdisciplinary nature of the approach, combining synthetic chemistry, microbiology, plant pathology, and computational biology.

Section 2: Impact (Approx. 5 pages)

This section must convince the evaluator that the project's success will have significant and far-reaching benefits for Europe.

- **Pathways to Impact:** Directly address the expected outcomes of the call HORIZON-CL6-2025-02-FARM2FORK-01. Create a clear table or list that maps the project's planned results to each of the call's four expected outcomes (e.g., "Result: Validated lead compound" maps to "Outcome: Cost-effective prevention

and control tools").

- **Scale and Significance of Project Outcomes:**
  - **Economic Impact:** Quantify the potential benefits. Reference the €5.5 billion annual threat and the 300,000 jobs at risk.[1] State that a successful product could not only save this value but also create a new, high-value market for a European-developed technology.
  - **Societal Impact:** Discuss the protection of cultural heritage (ancient groves), the preservation of rural livelihoods, and the restoration of farmer confidence in affected regions.
  - **Environmental Impact:** Argue that a targeted bactericide could reduce the need for broad-spectrum insecticides used for vector control, leading to positive outcomes for biodiversity and non-target organisms.
  - **Policy Impact:** Explain how the project's results will provide EU and national policymakers with a new, powerful tool, potentially leading to a revision of the current, purely defensive phytosanitary strategies.
- **Dissemination, Exploitation, and Communication:** Outline a preliminary but credible plan.
  - **Dissemination:** Mention plans for open-access publications, presentations at key scientific and agricultural conferences, and workshops for stakeholders.
  - **Exploitation:** State the clear intention to commercialize the results. Describe the plan to protect the IP through patents and the goal of bringing a product to market via the coordinating SME, potentially through licensing agreements with larger agrochemical companies.
  - **Communication:** Describe targeted communication activities for different audiences: policy briefs for regulators, practical guides for farmers, and public outreach to raise awareness.

This 10-page document must be a masterpiece of clarity and persuasion, presenting a self-contained and powerful argument for why this project, above all others, deserves to proceed to the next stage.

4.3 The Proposal (Stage 2 - Full Submission): Detailing the Implementation

Having successfully passed the Stage 1 evaluation, the full proposal builds upon the initial 10-page concept by adding comprehensive detail, particularly in the third evaluation criterion: **Quality and Efficiency of the Implementation**. At this stage, the anonymity is lifted, and the full strength of the consortium can be revealed. The

page limit is typically much larger (e.g., 45-50 pages), allowing for a granular description of the work plan.

Section 3: Quality and Efficiency of the Implementation (The New Section)

This section demonstrates that the consortium has the resources, expertise, and a logical plan to execute the project successfully.

- **Work Plan and Work Packages (WPs):** This is the heart of the implementation section. The project should be broken down into a series of interconnected Work Packages, each with clear objectives, tasks, deliverables, and milestones. A logical structure would be:
    - **WP1: Project Management and Coordination:** Led by your SME. Details the hybrid management structure, communication flows, risk management plan, and financial oversight.
    - **WP2: Rational Design and Synthesis of Novel Phosphinic Acid Library:** Led by your SME (specifically, your brother as the scientific expert). Describes the chemical synthesis methodologies, purification, and analytical characterization of the new compounds.
    - **WP3: *In Vitro* and Laboratory Screening:** Led by the university partner. Details the protocols for testing the synthesized compounds against pure cultures of *Xylella fastidiosa* (different subspecies) and on infected plant cell cultures to determine efficacy (MIC values) and phytotoxicity.
    - **WP4: Greenhouse Validation:** Led by the university or research organization partner. Describes the experiments on potted host plants (e.g., olive and almond saplings) in controlled environments to test the systemic uptake, translocation, and curative/preventative efficacy of the most promising lead compounds from WP3.
    - **WP5: "Living Lab" Field Trials:** Led by the research organization partner in collaboration with the farmer cooperative. Details the plan for small-scale, highly controlled field trials in affected regions (e.g., Italy, Spain) to test the best candidate formulations under real-world conditions. This WP is the cornerstone of the Multi-Actor Approach.
    - **WP6: Dissemination, Exploitation, and Communication:** Led by your SME, with strong support from all partners. Details the full plan for publications, stakeholder workshops, the IP management strategy (patenting), the business plan for commercialization, and public outreach.
    - **WP7: Ethics and Data Management:** A mandatory WP. Outlines how the project will adhere to ethical standards (e.g., in field trials) and manage its data according to FAIR (Findable, Accessible, Interoperable, Reusable)

principles, including plans for open data where appropriate.[48]

- **Consortium Description:** This is where you introduce your partners. For each partner, provide a detailed description of their organization, their specific expertise relevant to the project, and the key personnel who will be involved. The Partner Roles and Expertise Matrix (Table 4.1) should be included and elaborated upon here. Emphasize the complementarity of the partners—how their skills combine to cover the entire project value chain from basic chemistry to field application.
- **Budget and Resources:** Justify the requested lump-sum budget on a per-WP basis. Explain why the requested resources (person-months, equipment, travel, consumables) are necessary to achieve the objectives of each work package. The justification must be credible and demonstrate value for money.[48]

The full proposal must be a comprehensive and meticulously detailed operational plan. It must leave the evaluators with no doubt that the consortium is a world-class team with a clear, logical, and achievable plan to turn their ambitious idea into a tangible reality.

4.4 The Multi-Actor Approach in Practice: Integrating Stakeholders

A common weakness in Horizon Europe proposals is treating the Multi-Actor Approach (MAA) as a box-ticking exercise. A winning proposal demonstrates that stakeholder involvement is deeply embedded in the project's methodology and governance. The plan must show *how* different actors will contribute to and shape the project's direction at every stage.

A Practical Integration Plan:

- **Co-Design Phase (Proposal Stage):** Involve potential end-user partners (farmers, cooperatives) in the design of the field trial protocols (WP5) from the very beginning. Their input on practical constraints (e.g., application timing, compatibility with existing machinery, economic thresholds) will make the proposed research more relevant and credible. This co-design process should be explicitly described in the proposal.
- **Research and Development Phase (WP2-4):**
  - The **industrial formulation partner** should be involved early to provide feedback on the chemical properties of the synthesized compounds (WP2).

They can advise on which molecular characteristics are more likely to lead to a stable and effective final product, guiding the synthesis process towards commercially viable candidates.
    - An **Advisory Board** should be established, comprising representatives from the advisory/policy partner, the farmer cooperative, and the industry partner. This board should meet annually to review project progress and provide strategic guidance, ensuring the research remains aligned with practical needs and policy realities.
- **Testing and Validation Phase (WP5):**
    - The **farmer cooperative** and its members are not just passive hosts for trials; they are active research partners. They will be involved in applying the treatments, collecting observational data (e.g., on plant health, ease of use), and participating in workshops to interpret the results. This creates a "Living Lab" environment where innovation is tested and refined in a real-world context.[48] This direct engagement is a key success factor.
- **Dissemination and Exploitation Phase (WP6):**
    - **Farmers and advisors** are the most credible channels for disseminating results to the wider agricultural community. The project will empower them to become advocates by co-authoring practical guides, presenting at local farmer meetings, and participating in demonstration days held at the trial sites.
    - The **industry partner** will take the lead on developing the commercialization plan, leveraging their market knowledge.
    - The **policy-advising partner** will be responsible for translating the project's scientific findings into concise policy briefs for submission to national and EU-level plant health authorities.

By detailing these specific interactions within the work package descriptions, the proposal demonstrates a genuine commitment to the multi-actor philosophy. It shows that the project is not just conducting research *for* stakeholders, but *with* them, dramatically increasing the likelihood that its results will be adopted and have a real-world impact.

Part V: From Project to Profit - The Commercialization and IP Roadmap

5.1 Corporate Structure: Establishing Your R&D Startup

The foundation for monetizing the project's outcomes must be laid before the research even begins. The chosen vehicle for this is a dedicated Small or Medium-sized Enterprise (SME), which you and your brother will establish. This entity will not only serve as the project's coordinator but will also be the central hub for intellectual property ownership and future commercial activities.

Legal and Financial Establishment:
It is imperative to establish a formal legal entity (e.g., a limited liability company or its equivalent in your country of establishment) prior to the signature of the Horizon Europe Grant Agreement. The European Commission enters into a contractual relationship with legal entities, not individuals. This SME will be the official beneficiary and the recipient of the grant funding tranches. All financial transactions, hiring of personnel for the project, and contractual obligations will be managed through this company.
Defining Core Team Roles:
Within this startup, clear roles must be defined to ensure both scientific excellence and effective management. A logical structure would be:

- **Your Role: Chief Executive Officer (CEO) and Project Manager.** As the project manager, you will be the primary point of contact with the European Commission and the consortium partners. You will be responsible for the overall strategic direction, financial management (overseeing the delegated tasks), reporting, and driving the commercialization plan.
- **Your Brother's Role: Chief Scientific Officer (CSO).** As the lead scientific expert, he will be responsible for directing the research and development activities, particularly the design and synthesis of the novel compounds (leading WP2). He will be the primary author of scientific publications and will represent the project at technical conferences.

This clear division of labor, presented in the proposal, demonstrates a professional approach to both the research and the business aspects of the endeavor, instilling confidence in evaluators about the project's governance.

5.2 Intellectual Property Strategy: A Guide to Ownership, Protection, and Licensing

A robust intellectual property (IP) strategy is the single most important element for translating publicly funded research into a profitable business. The rules governing IP in Horizon Europe are designed to facilitate exploitation while protecting the interests of all partners. These rules are primarily defined in the Grant Agreement (GA) and must be further detailed in a private, legally binding Consortium Agreement (CA) among the partners.[61]

Understanding Horizon Europe IP Principles:

- **Background:** This refers to any data, know-how, or intellectual property held by a partner *before* the project begins that is needed to carry out the project or exploit its results. It is crucial that each partner declares their relevant Background in the Consortium Agreement. Access to Background must be granted to other partners on a **royalty-free basis** if it is needed for them to perform their tasks within the project. If it is needed to exploit their own results, access must be granted under **fair and reasonable conditions**, which can include financial compensation.[61]
- **Results:** This refers to any tangible or intangible output of the project, such as data, knowledge, and inventions. The fundamental rule is that **Results are owned by the beneficiary that generates them**. If two or more partners generate a result jointly and their respective contributions cannot be separated, they become **joint owners** of that IP.[61]

The Critical Role of the Consortium Agreement (CA):

While the GA sets the framework, the CA is where the detailed, commercially critical IP arrangements are negotiated. This agreement must be in place before the GA is signed. It is not just a legal formality; it is the foundational "shareholder agreement" for the future commercial venture. Key clauses to negotiate and define with extreme clarity include:

- A comprehensive list of each partner's Background IP.
- Precise rules for managing joint ownership, including who is responsible for patent filing costs and how decisions on licensing are made. Unless otherwise agreed, any joint owner can grant non-exclusive licenses to third parties, provided they give the other owners advance notice and fair compensation.[61]
- A clear process for reviewing publications and other disclosures to ensure that confidential information is not released prematurely and that patent applications can be filed first.

- First rights of refusal or specific licensing terms for partners wishing to use each other's Results.

Protection and Exploitation Strategy:

Horizon Europe obligates beneficiaries to use their best efforts to exploit their results. This includes an obligation to adequately protect results—for example, by filing for patents—if they are commercially viable.[61] The costs associated with patenting are eligible for reimbursement under the grant.

A viable strategy for this project would be:

1. **Core IP Ownership:** Your SME, as the leader of the chemical synthesis work package (WP2), will own the patents for the novel phosphinic acid compounds (the "active ingredients").
2. **Licensing-In:** You may license-in Background IP from the formulation partner to help develop the final product.
3. **Licensing-Out:** To reach the global market, your SME would likely license the patented compounds to a large, established agrochemical company with the global manufacturing capacity, distribution network, and experience to navigate the complex regulatory approval process in different jurisdictions. Your revenue would come from upfront payments, milestone payments, and royalties on sales.

This strategy allows your lean startup to focus on its core competency—R&D and IP generation—while leveraging the scale of a major player for commercialization.

5.3 The Path to Market: Mapping the Journey from Lab to Commercial Product

The Horizon Europe project is a crucial first step, but it is not the final one. A realistic commercialization plan must acknowledge the full development lifecycle, including the regulatory hurdles and the need for follow-on investment.

Mapping Progress with Technology Readiness Levels (TRL):

The TRL scale is a standard metric used by the EU to assess the maturity of a technology. The project should be designed to advance the technology through several levels:

- **TRL 1-2 (Start of Project):** Basic principles observed and technology concept

formulated. This is the stage of the initial idea.
- **TRL 3 (WP2/WP3):** Analytical and experimental proof of concept. Achieved when the first novel compounds show *in vitro* activity against *Xylella*.
- **TRL 4 (WP4):** Technology validated in the lab. Achieved when the compounds show efficacy in greenhouse trials on potted plants.
- **TRL 5-6 (End of Project - WP5):** Technology validated/demonstrated in a relevant environment. Achieved upon successful completion of the controlled field trials.

A successful RIA project will deliver a technology at TRL 5 or 6. Reaching the market (TRL 9) requires further development, full-scale manufacturing, and regulatory approval.

Navigating Regulatory Hurdles:

The registration of a new plant protection product in the EU is a lengthy and expensive process, governed by stringent regulations. The proposal should demonstrate foresight by including a specific task within WP6 to map the complete regulatory pathway for a new active substance. This shows evaluators that the consortium understands the real-world challenges beyond the lab and is planning for them. This may involve consulting with regulatory affairs specialists.

Securing Post-Project Funding:

The €6 million from Horizon Europe is intended to de-risk the technology to the point where it becomes attractive to private investors. The business plan developed in WP6 should explicitly detail the strategy for securing follow-on funding to take the product from TRL 6 to TRL 9. This could come from:

- **Venture Capital (VC) firms** specializing in ag-tech or green chemistry.
- **Corporate venture arms** of major agrochemical companies.
- **Further EU funding instruments** designed for scaling up, such as the EIC Accelerator.

The successful completion of a Horizon Europe project provides immense validation and significantly increases the attractiveness of the startup to these next-stage funders.

5.4 Post-Project Valorisation: Leveraging EU Resources for Market Entry and

Scaling

The European Commission's support for innovation does not cease when the final project report is submitted. A suite of dedicated services exists to help successful projects bridge the "valley of death" between research and market. A forward-thinking proposal will include a plan to actively engage with these services.

Key EU Support Mechanisms for Commercialization:

- **Horizon Results Booster (HRB):** This is a free service provided by the Commission to consortia of EU-funded projects to help them with their exploitation strategy. Services include business plan development, support for patenting and licensing, and assistance in finding investors or partners. The project should plan to apply for HRB services towards the end of its term to refine the commercialization strategy developed in WP6.[64]
- **European IP Helpdesk:** This service offers free, first-line support and training on all aspects of intellectual property management in EU projects. It is an invaluable resource for an SME navigating the complexities of the Consortium Agreement and patenting strategy.[65]
- **European Innovation Council (EIC) Accelerator:** This is the logical next step in the EU funding pathway. The EIC Accelerator is specifically designed for high-potential SMEs and startups to scale up their game-changing innovations. It offers a unique blend of funding: a grant component of up to €2.5 million to cover further development (e.g., large-scale trials, regulatory dossier preparation) and an equity investment component of up to €15 million to fund market entry and scaling. Having successfully completed a Horizon Europe RIA project is a powerful track record that significantly strengthens an application to the EIC Accelerator.[67]
- **Horizon Results Platform:** This is a showcase for EU-funded research results, connecting innovators with investors, partners, and policymakers. The project's key exploitable results should be actively promoted on this platform to maximize visibility.[65]

Learning from Success Stories:

The path from EU project to commercial success is well-trodden. Referencing successful examples demonstrates that this ambition is realistic. For instance, the Greek SME **AgroApps** strategically used its participation in Horizon 2020 projects to develop and commercialize a suite of digital agriculture services, securing long-term

partnerships with major players in the agrifood industry.[68] Similarly, companies like

Lallemand and **Evonik** have successfully commercialized biotechnology products, such as specialized yeasts and probiotics, that originated from R&D efforts, some of which were supported by the EU ecosystem.[69] These cases show that with a clear vision, a strong IP strategy, and strategic use of the available support mechanisms, it is entirely feasible to transform a Horizon Europe project into a thriving, profitable business that delivers significant value to the European economy and society. The proposal should conclude by positioning this project as the first step on this proven pathway to impact.

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