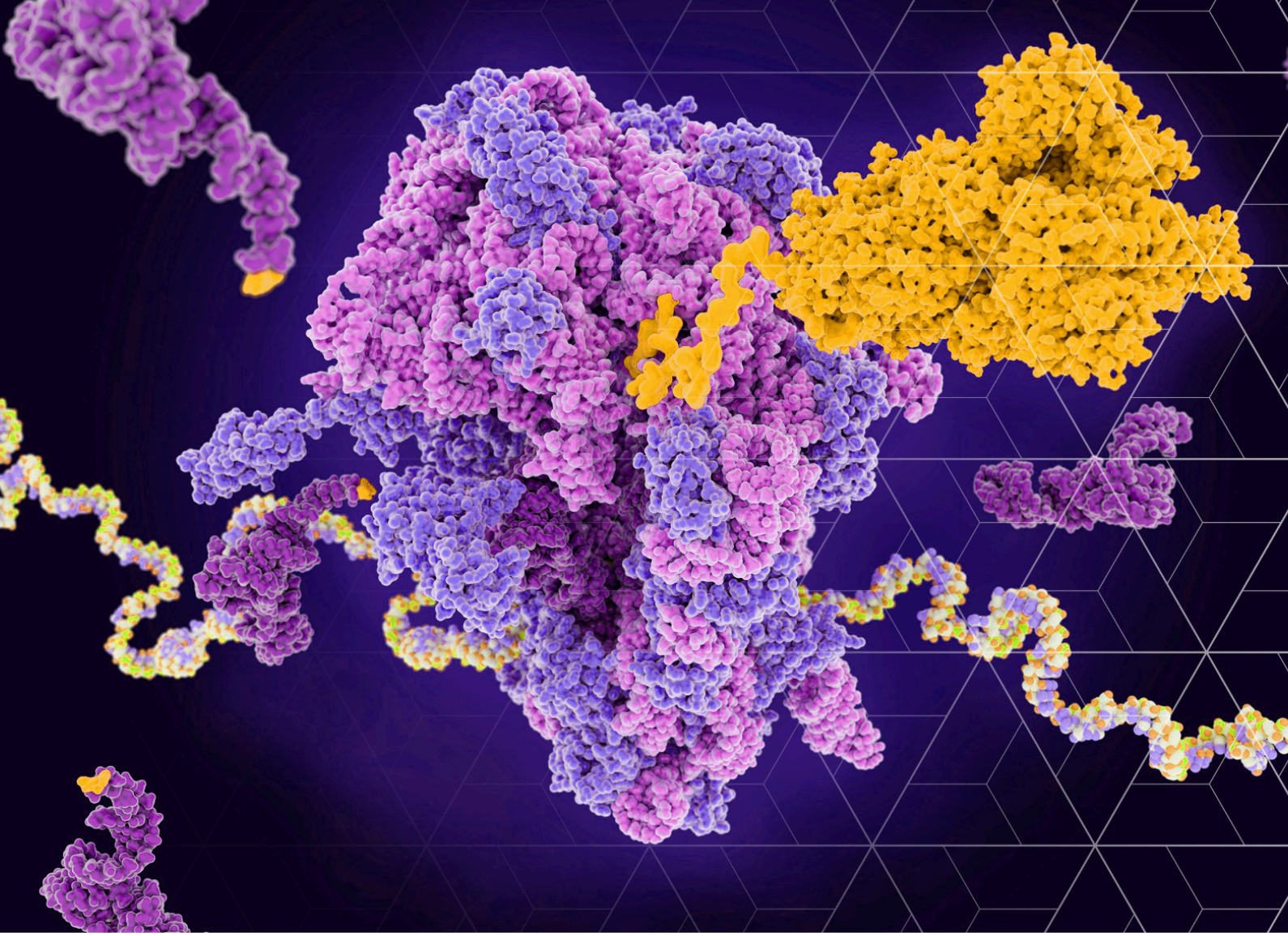

Participation in the Mutation-Specific Codon Suppression for Aging and Longevity IP-NFT

V1.1 - May 23, 2024

with ARTANBIO

VitaDAO

vitadao.com

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Notice

This crypto-asset white paper has not been approved by any competent authority in any Member State of the European Union. The offeror of the crypto-asset is solely responsible for the content of this crypto-asset white paper.[1]

[1] Pursuant to MiCA, Title II, Article 6, paragraph 3

Foreword

This whitepaper is to be used exclusively to offer participation in the governance and funding of the project and resulting intellectual property represented by an IP non-fungible token (IP-NFT), as described in the subsequent sections, through the issuance and placement of IP Tokens (IPTs) in a manner consistent with European regulations.

At the current time, IP-NFTs are not, based on the latest legal advice, considered to be securities or financial instruments. However, the current regulatory regimes are fluid and a future legal or regulatory change in one or more jurisdictions may alter the classification of either IP-NFTs or IPTs.

To that end, VitaDAO has taken the view that without prejudice to, or election of, jurisdiction it is desirable to provide disclosures in good faith, such that a competent authority would find this whitepaper to materially meet the requirements of EU guidance under the Markets in Crypto-assets (MiCA) regulation (EU) 2023/1114 and amending Regulations (EU) No 1093/2010 and (EU) No 1095/2010 and Directives 2013/36/EU and (EU) 2019/1937 as known, and amended, as of the date of issuance.

Important statement from the governance function of VitaDAO[2]

This whitepaper complies with Title II of Regulation (EU) 2023/1114 on markets in crypto-assets (MiCA), and, to the best of the knowledge of the governance function of VitaDAO, the information presented in this whitepaper is fair, clear and not misleading, and this whitepaper makes no omission likely to affect its import.

[2] Pursuant to MiCA, Title II, Article 6, paragraph 6

Part I: IP Tokens and Regulatory Requirements

I.1 Notices and Disclosures

1. *Primacy of Document.* This whitepaper supersedes all previous communications regarding the project, the associated IP-NFT and the proposed IP Tokens (IPTs).

2. *Primacy of Issuer.* No parties are authorised to make representations or warranties in addition to, or contrary to, those made by the Issuer in this whitepaper with respect to the IP-NFT, or IP Tokens (IPTs) described herein.

3. *Primacy of Source Material.* All descriptions and summaries of documents in this whitepaper are for convenience, and are qualified by the actual documents cited. The reader should ensure they review the original documents prior to making any decisions regarding participation in the governance and funding of the project through holding of IP Tokens (IPTs).

4. *Not Construed as Advice.* This whitepaper does not purport to offer financial, business, taxation or legal advice. As each participant's circumstances are unique, there should be no reliance on the Issuer or Offeror's legal counsel as providing advice for a participant's particular circumstances. Participation should be contemplated in conjunction with independent legal advice provided to a participant with full knowledge of their business or personal situation.

5. *Right to Change or Withdraw.* The Issuer reserves the right to modify or withdraw this offer to participate subject to the reciprocal right of a potential participant to ask questions and receive information as to the nature of any changes.

6. *Business of the Issuer.* VitaDAO is a decentralised autonomous organisation (DAO). DAOs do not have the distinct legal personality possessed by individuals, companies, or other legal entities. Rather, DAOs are holders of tokens (tokenholders), who participate in the management and decision-making of the entity by collectively casting votes. This bottom-up decision making in a DAO replaces the usual top-down decision making by the board of a company. All the voting and activity of the DAO are recorded in, and viewable via the blockchain.

   VitaDAO, as the Issuer, is a funder and provider of commercialization services to early-stage longevity research projects and provides support to longevity science researchers. VitaDAO welcomes the participation of the research community and other interested stakeholders through the sharing of governance rights, represented by IP Token crypto-assets. More information on VitaDAO can be found online at https://www.vitadao.com/.

Financial disclosures regarding VitaDAO are attached as *Appendix B*.

7. *Governance / Management Function of VitaDAO.* VitaDAO, as a Decentralised Autonomous Organization (DAO), has no central authority, but is governed by the publication of a series of proposals which are voted upon by the holders of VitaDAO's native token – VITA (ISO 24165 DTI: HZ2L1PBPC).

   VITA is a governance token with no assigned economic rights in the estate of VitaDAO. The tokens are provided in recognition of one or more of: service delivery and outcomes, financial support, or support for the longevity science ecosystem as a whole. The latter may be recognized based on strategic and subjective criteria. Collectively, the distribution of VitaDAO's native token forms a reputation-based system of governance based on proof-of-stake in the organisation and its stated mission.

   Once a governance proposal is issued, the community votes on the proposal and the results of the vote dictate VitaDAO's actions. The decision and any resulting actions from any particular proposal is then executed by a group of service providers ("pods") coordinated through pod leaders.

   Pod Leaders are provided operational decision-making authority to execute the decisions of the VitaDAO tokenholders. Policies and governance on operational matters including, but not limited to, spending authority, travel expense policies, fee-for-service compensation, treasury management and fundraising activities - which includes the issue of IP Tokens - are all approved by the VItaDAO tokenholders prior to execution by the pods.

   VitaDAO's governance proposals as well as voting results are generally publicly available at https://gov.vitadao.com/ and on the Snapshot voting platform. The governance attached to this issue of IP Tokens are found in Appendix C.

8. *Further Information.* If you have questions, concerns, or require further information in connection with this offer to participate, you can contact VitaDAO as follows:

   VitaDAO Global Services, Inc.
   3456 Paul Anka Drive,
   Ottawa, Ontario CANADA K1V 9K6

   E-mail: ipt-information@vitadao.com

9. *Forward-looking Statements.* This whitepaper contains forward-looking statements based on estimates and assumptions. Forward-looking statements include, among

other things, statements concerning the project, future financial needs, results of operations and prospects of the Issuer. These statements usually contain the words “believes”, “plans”, “expects”, “anticipates”, “intends”, “estimates” or other similar expressions. For each of these statements, you should be aware that forward-looking statements involve known and unknown risks and uncertainties. Although it is believed that the expectations reflected in these forward-looking statements are reasonable, there is no assurance that the actual results or developments anticipated will be realised or, even if realised, that they will have the expected effects on the project or associated financial conditions, results of operations or prospects of the project team or Issuer.

These forward-looking statements speak only as of the date on which the statements were made, and no obligation has been undertaken to publicly update or revise any forward-looking statements made in this whitepaper or elsewhere as a result of new information, future events or otherwise, except as required by applicable laws and regulations.

Participants are cautioned not to place undue reliance on these forward-looking statements, which are subject to risks and uncertainties that could cause actual results to differ materially from those expressed or implied in the forward-looking statements. Before making any decisions, prospective participants should carefully consider the risks and uncertainties described in this whitepaper and consult with their own legal, financial, and tax advisors.

10. *Restrictions on Participation.* The following restrictions applies to participation in the governance and funding of this project by holding IP Tokens:

a. The IP Tokens described herein are not being offered or sold to "U.S. persons" (within the meaning of Rule 902 of Regulation S promulgated under the Securities Act of 1933, as amended) or within the United States of America and may not be offered or sold, directly or indirectly, to U.S. persons or within the United States of America, unless, among other things, they are subsequently registered under applicable securities laws or an exemption from such registration is available.

b. Further, no entity, person or body corporate, nor any affiliates or beneficial owners of the same, who is deemed a Prohibited Person may own, buy, or sell the IP Tokens described herein. For the purposes hereof, "Prohibited Person"means any individual, or legal entity or person, including a government or political subdivision or an agency or instrumentality thereof (each a "Person") that is: (i) a national or resident of, or legal entity formed or incorporated within or subject to the Laws of any United States embargoed or restricted country, (ii) a national or resident of, or legal entity formed or incorporated within or subject to the Laws of the Republic of Cuba, Democratic People's Republic of North Korea, Islamic Republic of Iran, Libya, People's Republic of China, Republic of South Sudan, Republic of Sudan, Syrian Arab, Republic or the Crimea; (iii) included on, or affiliated with any Person on the United States Commerce Department's Denied Persons List, Entities List, or Unverified List; the U.S. Department of the Treasury's Specially Designated Nationals and Blocked Persons List, Specially Designated Narcotics Traffickers or Specially Designated Terrorists, or the Annex to Executive Order No. 13224; the Department of State's Debarred List; or UN Sanctions; (iv) a Person with whom business transactions, including exports and re-exports, are restricted by a United States Governmental Authority, including, each item listed in the foregoing clauses (i), (ii), (iii) and (iv) and any updates or revisions thereto and any newly published rules therefore; or (v) a subject or target of any other economic sanctions administered or enforced by the United Nations, the European Union or the United Kingdom.

I.2 IP-NFTs and IP Tokens (IPTs)

A Blockchain is a decentralised digital ledger technology that allows for secure and transparent record-keeping of transactions. Since the publication of the Bitcoin whitepaper in 2008 by the pseudonymous person or group known as Satoshi Nakamoto, blockchain technology has gained significant attention and adoption and spawned a whole ecosystem of cryptocurrencies and blockchain technology, leading to new innovations and use cases beyond just currency.

Non-fungible tokens (NFTs) are a type of digital asset that uses blockchain technology to verify and authenticate ownership, uniqueness, and provenance. NFTs can be used to represent various forms of digital content, including art, virtual real property, scientific research and development (R&D) data, and intellectual property. They provide a new way to manage and protect intellectual property, allowing creators and owners to easily transfer ownership, establish authenticity, and control usage rights.

NFTs are a feature of the Ethereum blockchain and are described in the technical specification ERC-721 and ERC-1155, as amended and published by the Ethereum Foundation (https://ethereum.org/)

IP-NFTs (Intellectual Property Non-Fungible Tokens) are a specific type of NFT based on the above standards that represent intellectual property and data rights to scientific research. IP-NFTs attach legal contracts, such as sponsored research agreements, data, patents and other commercially relevant documents encoded to NFT smart contracts providing a new asset class.

An IP-NFT can be transferred peer-to-peer, made composable with DeFi, used to distribute governance to groups of stakeholders, built upon to unlock new ways to interact with and develop IP, R&D data, and NIPIA (Non-IP Intangible Assets, like trade secrets and publicity rights), used to empower stakeholder enforcement of ethics in commercialization, and create liquidity in IP markets through the development of this new asset class..

The first IP-NFTs were minted by Molecule AG for the VitaDAO community in 2021 to register its longevity therapeutics IP and R&D data rights on the Ethereum blockchain.

IPTs (IP Tokens) are fungible tokens mintable by IP-NFTs in order to distribute rights and responsibilities to the IP and R&D data of IP-NFTs to groups of token holders, incentivizing a community to co-develop and co-govern the attached research.

The first IPTs, VITA-FAST, were minted by VitaDAO using the Korolchuk IP-NFT for the Korolchuk project developing autophagy activators.

These IPTs represent membership in an IP pool containing the IP and R&D data attached to the parent IP-NFT.

The rights of IPT holders are governed by an IPT Membership Agreement specific to each IP-NFT project. Those rights include, minimally:

- *Governance:* IPT holders have the right to participate in the governance of the IP-NFT and its development. This includes voting on proposed licences and uses of proceeds.

- *Access to Intellectual Property:* IPT holders have access to relevant data and other Intellectual Property (IP) or future Intellectual Property arising from the development of the IP-NFT. This is necessary for due diligence and to govern the development of the IP-NFT intelligently. However, this does not grant any licence to the IP.

- *Duty of Care:* IPT holders have a Duty of Care to honour, support, and adhere to the terms and conditions of the associated IPT Membership Agreement, including any governance agreement made pursuant to it.

- *Confidentiality:* IPT holders must not, without consent, use or disclose any confidential information or IP for any purpose or attempt to sell or register any Confidential Information, IP, or R&D data rights developed through participation in the IP pool.

- *Governance of Economic Proceeds:* IPT holders do not have predetermined economic rights in the IP-NFT or underlying IP. Rather, IPT holders have the right to govern the manner and distribution of proceeds from any sale or revenues derived from the IP, subject to regulatory and taxation requirements as may be in force at the time the decision to disburse proceeds is made. Each IPT agreement outlines the manner in which these rights may be governed and exercised. Please note that IPT holders will not be able to distribute proceeds from the sale or licensing of the underlying IP-NFT directly to themselves; rather IPT holders would either need to opt for the right to issue a new asset referenced token governing those economic proceeds, or otherwise consider participation in a profit sharing scheme, in each case in compliance with any additional legal and/or regulatory requirements applicable in respect of such tokens or schemes.

- *Exercise of the rights and obligations of IPT holders*: IPT holders may exercise their rights and obligations, or modify those rights and obligations in accordance with the IPT Membership Agreement attached as *Appendix A*.

Important Notices

- IP Tokens may lose their value in part or in full.
- IP Tokens may not always be transferable.
- IP Tokens may not be liquid.
- IP Tokens are not covered by the investor compensation schemes under Directive 97/9/EC of the European Parliament and of the Council , or the deposit guarantee schemes under Directive 2014/49/EU.

Part II: The Project

This summary should be read as an introduction to this document only. The prospective participant should base any decision to participate in the governance of the project by holding IP Token crypto-assets on the contents of this document as a whole and not on the summary alone.

This offer to participate in the governance of the project by holding IP Tokens does not constitute an offer or solicitation to purchase financial instruments and any such offer or solicitation can be made only by means of a prospectus or other offer documents pursuant to the applicable national law.

This crypto-asset white paper does not constitute a prospectus as referred to in Regulation (EU) 2017/1129 of the European Parliament and of the Council or any other offer document pursuant to European Union or national law.

II.1 Offer to Participate – At a Glance

Issuer:	Vital Artan Holdings, Limited
Ethereum Address:	vitarna.eth (0x452f3b60129FdB3cdc78178848c63eC23f38C80d)
Registration Date:	January 26, 2024
Mailing Address:	Inniscarra, Main Street, Rathcoole Co Dublin IRELAND D24 EO29
LEI :	984500EA038D6XCAEB33
Registry ID:	756576 (Ireland)

Offerer:	Vital Artan Holdings, Limited
Ethereum Address:	vitarna.eth (0x452f3b60129FdB3cdc78178848c63eC23f38C80d)
Registration Date:	January 26, 2024
Mailing Address:	Inniscarra, Main Street, Rathcoole Co Dublin IRELAND D24 EO29
LEI :	984500EA038D6XCAEB33
Registry ID:	756576 (Ireland)

Issuer	Vital Artan Holdings, Limited
Date of Issue	April 16, 2024
Date of Notification	February 1, 2024
Crypto Asset	VITARNA Token
Applicable Law	Switzerland
Competent Court	Switzerland
Denomination Amount	WETH
Issue Price	0.000079 WETH
Offering Size	1 000 000 VITARNA tokens
Current Supply[3]	5 000 000 VITARNA tokens
Minimum Investment	N/A
Minimum Target Size	79 WETH
Maximum Offering Amount	79 WETH
First Issue Date	May 23, 2024
Final Issue Date	June 6, 2024
Trading Platform	Molecule AG Marketplace
Issue Period	Participants may bid on the IPTs from the First Issue Date until the Final Issue Date as long as the total Maximum Offering Amount has not been reached (the "Issue Period").
Underlying Governed Assets	Mutation-Specific Codon Suppression for Aging and Longevity IP-NFT
Limited Recourse	Governance rights per associated IPT Agreement

[3] *As of the Date of Notification.*

Agents, if any	Molecule AG
Taxation	N/A
Restrictions	1. Purchase, sale, or transfer to US and Prohibited Persons [Part 1, Section I.1, 10(b)]; 2. Number of participants not to exceed 499; 3. Total funds raised not to exceed 5m Euro or equivalent.
Investor Eligibility	Issued to current VITA Tokenholders only.
Form of Issuance	ERC-20 Token on the Ethereum blockchain
Risk Factors	Purchasing IPTs involves risks. See "Risk Factors".
Fees and Expenses	The Issuer will finance any and all present or futures fees, costs, expenses required to be provisioned or paid by the Issuer arising in connection with the Offering and the Crypto Assets and/or required to be provisioned or paid for by the Issuer in order to preserve the existence of the Issuer, to maintain it in good standing or to comply with applicable laws, as well as operational costs, external advisory, and other discretionary expenses. All prospective purchasers of the IPTs will be responsible for their own costs, fees and expenses including any gas fees, as well as the costs, fees and expenses of their legal counsel and other advisors. Each purchaser of the IP Tokens shall indemnify the Issuer for any finder's fee for which such purchaser is responsible.
Specified Currency	The IPTs issue price is denominated in Wrapped Ether or "WETH" (ISO 24165 DTI: 1FRZDTR6N).

This whitepaper presents the funding of longevity research through the sale of VITARNA IPTs, which are ERC-20 compliant tokens on the Ethereum blockchain.

The VITARNA tokens represent fractions of governance rights that may be exercised over the Mutation-Specific Codon Suppression for Aging and Longevity Non-Fungible Token (IP-NFT) which contains the outcomes of the work funded by VitaDAO in ArtanBio. This offers a novel mechanism for public involvement in the decision-making processes. In return, the crowdsale of tokens is intended to financially support the longevity research activities of ArtanBio.

The sale of VITARNA tokens represents an innovative approach to democratising funding for scientific research, however it demands thorough understanding and careful consideration of potential risks for potential VITARNA token buyers.

The purchase of VITARNA tokens inherently carries risks including the unpredictable nature of research outcomes which may impact the future value of the project, regulatory changes and uncertainties, and challenges related to intellectual property rights enforcement. The VITARNA token primary issuance is offered via the Molecule AG platform, operating under the laws of Switzerland.

The subsequent sections of this whitepaper will delve deeper into the various aspects to offer a comprehensive view of this research funding initiative.

II.2 Project Overview

The process of aging is closely related to the accurate reading, writing, and copying of DNA. Genomic instability, which results in DNA blueprint mutations, is a key factor that can reduce the amount of mRNA in cells (insert ref: López-Otín, Carlos et al. Cell, Volume 153, Issue 6, 1194 - 1217.) This reduction can lead to the malfunction of proteins that regulate vital processes, such as DNA repair, epigenetic regulation of protein expression, and the reduction of tumour suppressors. These suppressors play a crucial role in preventing the development of cancer. Mutations in nucleotides that result in nonsense or stop mutations are a common pathway leading to the events described above. The numerous pathologies that result from accumulated nonsense mutations have solidified genomic instability as a core hallmark of aging [1].

Artan Bio has proposed a novel approach to address genetic and age-related diseases caused by nonsense mutations. These mutations lead to premature protein translation stops, resulting in incomplete and nonfunctional proteins. The solution involves an engineered suppressor system that recognizes these codons and restores normal protein translation. This technology, delivered through clinically validated modalities, shows promising preliminary results and offers various clinical opportunities.

VitaDAO initially supported Artan Bio with funding to design and validate their engineered suppressor system (VDP-103) in cells with targetable mutations to confirm validity of the approach.

Having successfully completed the aims of VDP-103, Artan Bio seeks to continue the development of the engineered suppressor system. The sale and funds aim to continue to support the work initiated by Artan Bio, further validate the system in animal models to support preclinical translation, and establish a development candidate for use in clinical trials.

II.3 The Team

Michael Torres, Ph.D., PI, is a highly accomplished biotechnology professional with extensive experience in cancer therapeutics, drug discovery, and molecular biology. As an Entrepreneur at The Accelerator for Cancer Therapeutics, Texas Medical Center(TMC), Dr. Torres engages with high-impact cancer therapeutic projects, develops networks, and creates resources to support product development. Dr. Torres has played a pivotal role in transforming another academic project into a VC-backed company, ReCode Therapeutics, which has raised $80M from prominent investors and secured a $3.2M award from the CF Foundation.

With a strong background in research and development, he has held the position of VP of R&D at ReCode Therapeutics, Inc., where he directed cross-functional teams, managed therapeutic programs, and facilitated the preclinical development of novel RNA LNP drug products. Dr. Torres has also contributed significantly to the field through his work as a Postdoctoral Fellow at UT-Southwestern, investigating novel therapeutics for treating Cystic Fibrosis. Dr. Torres received his Ph.D. in Cancer Biology at UT-Southwestern Medical Center at Dallas.

With a proven track record in research and business development, Michael Torres has a keen understanding of the biotechnology landscape and is dedicated to advancing novel therapeutics for the betterment of patients worldwide.

Anthony Schwartz, Ph.D., VitaDAO EIR PM, is an entrepreneur with over 20 years of experience in biotechnology-based startup companies. Dr. Schwartz has started at least 20 startups primarily focused on cancer, rare diseases, and aging, leading to large financings and FDA approval. He has significant expertise in cancer immunotherapies, particularly antisense, small molecules, and CART therapeutic modalities.

During his career, Dr. Schwartz has served in executive positions in several biotechnology companies. More recently, he was part of Hibiscus BioVentures, which facilitated financings and launched several biotechnology companies. He helped establish the Mayflower BioVentures fund, which spearheaded laboratory-stage therapeutic assets from the Mayo Clinic into companies. Additionally, he serves as an advisor to the management teams and boards of numerous small biotechnology companies, including Primera Therapeutics, Sendero Biotechnology, Abvance Therapeutics, Brisight Biosciences, Matrix Biosciences, Morphiex Biotherapeutics, and joined the VitaDAO team in Q2'2023.

Dr. Schwartz received his Ph.D. in biomedical engineering from Colorado State University, with research focused on the immune system's role in cancer, novel radiation therapies, and stem cells. He later became an NIH/NCI postdoctoral fellow, where he focused on CD47-based immunotherapies for cancer, which led to the launch of Morphiex Biotherapeutics. Dr. Schwartz has been published in multiple prestigious journals and holds patents on a class of drugs attenuating the immune system for treating cancer and diabetes. Finally, he is a professor at Johns Hopkins University, teaching a course on finance and how to launch a biotechnology company.

In addition to the core team outlined above, the project has support from the entire VitaDAO community of contributors.

II.4 Project Background

Nonsense mutations contribute significantly to a wide range of genetic and age-related diseases by inducing premature stops of protein translation when occurring in coding regions.

Dr. Torres, an RNA expert and co-founder of ReCode Tx, proposed an engineered suppressor tRNA that can specifically recognize these codons and restore normal protein translation. Delivery can be achieved using to-be-determined clinically-validated drug delivery vectors, including adeno-associated viral (AAV) vectors . This technology has shown promising preliminary results, with several possible clinical opportunities. A stepwise research plan is outlined to confirm the feasibility and identify the most promising clinical applications.

Problem

A nonsense mutation is a point mutation in a sequence of DNA or RNA that results in a premature termination codon (PTC) or a nonsense codon, leading to a truncated, incomplete, and nonfunctional protein product.

Nonsense mutations are the underlying molecular pathology in approximately 10% of patients with genetic diseases like cystic fibrosis. They are also implicated in age-related diseases, like cancer [5, chapter 2].

Nonsense mutations at arginine CGA codons resulting in the stop codon, UGA (one of the three stop codons in the genetic code), caused by hydrolytic deamination of 5-methylcytosine at CpG sites, occur frequently in tumour suppressor genes [2].

Different strategies have been attempted so far to mitigate the effects of nonsense mutations [7, 8]:

Nonsense-Mediated mRNA Decay (NMD) Inhibition by Drugs . NMD is a highly conserved pathway for the surveillance and degradation of abnormal mRNAs, identified based on premature termination codons. Drugs that block NMD can activate PTC readthrough, as is the case for aminoglycosides, such as G418 and NB-124, or PTC-124 (Ataluren). The drawbacks of this approach are low efficiency, the incorporation of near-cognate amino acids at PTC, and readthrough at natural termination codons (NTC), resulting in aberrant protein products and small therapeutic windows.

Pseudouridylation . Unlike NMD inhibition, which targets any PTC, a pseudouridylation drug can be tailored to a specific disease-causing PTC. Unlike aminoglycosides, pseudouridylation raises little concern about global NTC readthrough, mitigating potential off-target activity. However, like aminoglycosides, it promotes the misincorporation of near-cognate amino acids.

Solution – Engineered Suppressor System

Nonsense mutations can be suppressed by a mutation in the anticodon sequence of a tRNA molecule so that it recognizes the stop codon instead. The figure below shows how such a “suppressor tRNA” works to suppress the effect of the mutation of a glutamine codon into an amber nonsense stop codon.

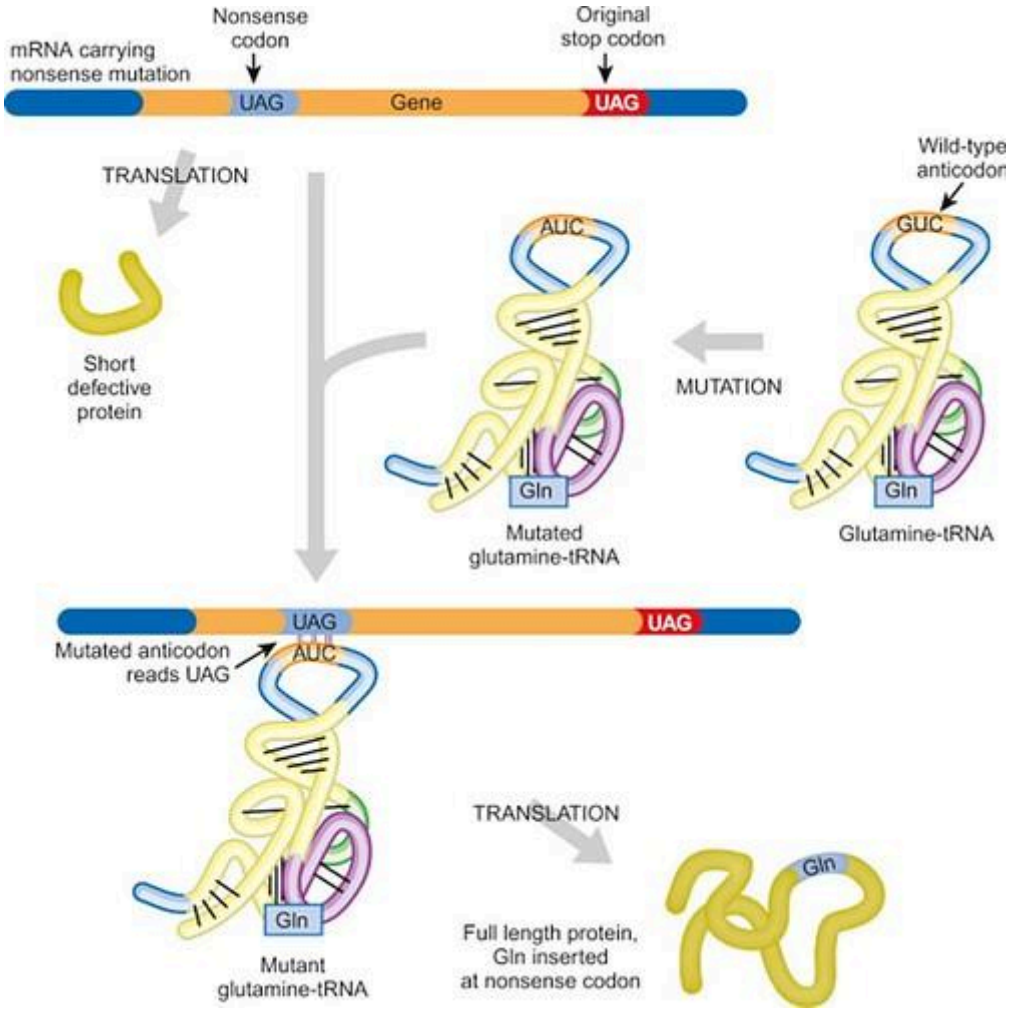


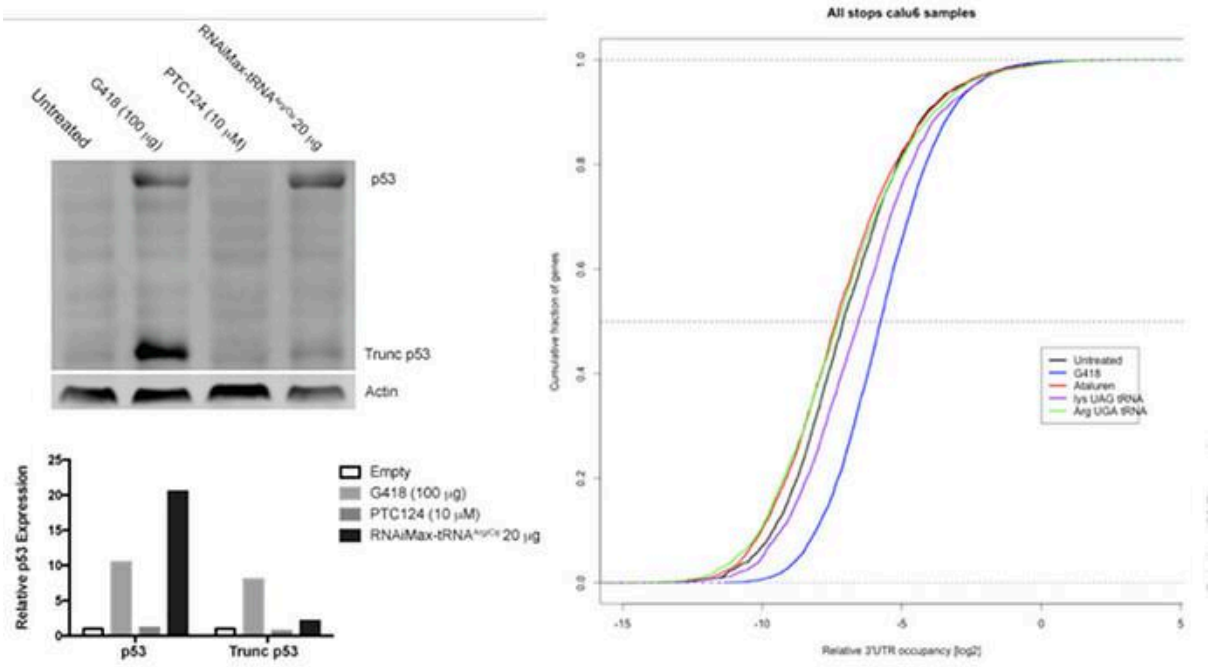
Figure.Mechanism of suppression of a nonsense amber codon [4]

Similarly, an opal suppressor tRNA can recognize the premature stop codon caused by a nonsense mutation in the CGA codon, allowing for the incorporation of specific amino acid at that position and the production of a full-length protein.

While suppressor tRNAs occur naturally due to mutations, they can be detrimental because they imply partial loss of translation capability for a given amino acid, which can be lethal in insects and mammals. In addition, naturally occurring suppressor tRNAs bind with nonsense and normal stop codons, generating longer (and incorrect) versions of many proteins whose genes were never mutated. [4]

Artan Bio proposes an engineered arginine suppressor tRNA capable of specifically targeting nonsense opal codons without competing with normal tRNA.

Preliminary ribosome profiling data were obtained with collaborators at Johns Hopkins that show rescue of TP53 levels in calu6, a cell line with an opal nonsense mutation in the gene (homozygous TP53 R196X), without significant NTC readthrough, performing better than known alternative interventions. See the figure below.



[image940×525 48 KB]

In this experiment, cells were treated with G418 (a drug that significantly causes read-through), Atalruren (or PTC124) (PTC therapeutics readthrough drug), the lysine amber suppressor, and the arginine opal suppressor. The tRNAs were oligos delivered by RNAiMax. The western blot shows that G418 and Arg/Op rescued p53, but G418 had more truncated p53 than Arg/Op suggesting it is not specific. PCT124 failed to rescue p53 in this experiment.

The graph is a genome-wide ribosomal profiling study using Calu6 cells with the indicated treatments. The degree of right shifting indicates read-through beyond normal stops (into the 3' UTR). The data demonstrate that G418 reads through normal stops, as does lysine/amber, to a certain extent, while the arg/opal tRNA does not. PTC124 either, but that's not surprising, given the drug history and our data.

Drug delivery

Artan Bio is prioritising viral vectors to deliver the engineered suppressor system. Amongst the viral vectors, AAV9 is a promising vector for clinical use due to its ability to efficiently transduce various tissues and organs, including the heart, liver, skeletal

muscle, and central nervous system (CNS). AAV9 has been shown to have higher transduction efficiency in the CNS than other AAV serotypes, making it an attractive vector for treating neurological disorders.

AAV Serotype	Primary Target Tissue	Approx. Number of Clinical Trials	Approx. Success Rate in Clinical Trials
AAV1	Muscle, heart	~30	~60%
AAV2	Retina, brain, liver	~100	~65%
AAV5	Retina, brain, liver, lung	~20	~55%
AAV6	Muscle, heart, lung, brain	~10	~50%
AAV8	Liver, muscle, retina, CNS	~50	~70%
AAV9	CNS, heart, liver,	~60	~75%

image451×791 44.9 KB

In particular, AAV9-based gene therapies have shown promising results in clinical trials for treating SMA, a neuromuscular disorder caused by mutations in the SMN1 gene. AAV9-mediated gene therapy for SMA has been shown to increase the levels of SMN protein and improve motor function in patients.

Thus, the lead therapeutic approach would be to use AAV9 to deliver an arginine opal suppressor. Given the validity of AAV9, this would enable us to optimise our path to first-in-human studies upon successful generation and validation of lead candidates. We could develop an oligo-based approach as a backup.

Opportunity

The rate of nonsense mutations among pathologies is variable. However, the gene silencing mechanism occurring due to a nonsense mutation is shared. Consequently,

common therapies can be applied to patients with various diseases, with an enormous pipeline-in-a-pill potential, as is characteristic of candidate longevity interventions.

This potential has attracted several startups that have raised significant investments in recent years, such as, in the tRNA space: Alltrna [10], hC Bioscience, ReCode Therapeutics (co-founded by this project's PI), and Tevard [7].

Some of the diseases implicated with nonsense mutations are Duchenne muscular dystrophy (DMD), cystic fibrosis (CF), spinal muscular atrophy (SMA), cancer, metabolic diseases, and neurologic disorders.

Artan Bio would determine lead indications with in vivo assessments in disease models. At this point, the company does not intend to focus on treating a specific disease like SMA but to generate a therapy guided toward globally suppressing arginine opal mutations that occur in multiple genes in parallel (see table below).

Table 1 Predicted epigenetic-mediated nonsense mutations in human genes (set 1) involved in aging and concomitant diseases, and the potential of cognate transcripts to be targeted by NMD

Transcripts of genes	Transcript accession	Total number of codons	Number of CGA codons—source of PTC		Number of introns in CDS	Number of SECIS-like elements	Number of CGA codons upstream of SECIS
			Total	Eliciting NMD			
ADIPOQ-1	NM_001177800	244	1	0	1	1	1
APOCIII	NM_000040	99	1	1	2	0	0
APOE	NM_000041	317	0	0	1	0	0
APP-1	NM_000484	770	8	8	17	3	5
ATM-1	NM_000051	3056	21	20	61	3	21
BLM-1,2	NM_000057	1417	3	3	20	0	0
	NM_001287246						
CAT	NM_001752	527	2	2	12	0	0
CYP1A1	NM_000499	512	2	2	4	0	0
CYP1B1	NM_000104	543	2	2	2	0	0
DKC1-1	NM_001363	514	7	7	14	0	0
ERCC2-1	NM_000400	760	3	3	21	0	0
ERCC2-2	NM_001130867	405	3	3	10	0	0
ERCC5	NM_000123	1186	7	4	14	2	7
ERCC6	NM_000124	1493	15	14	19	1	0
ERCC8-1	NM_000082	396	1	0	12	0	0
FANCA-1	NM_000135	1455	6	6	42	1	6
FANCA-2	NM_001018112	297	1	1	10	0	0
HSPA1A	NM_005345	641	2	0	0	0	0
Lamin A-1	NM_170707	702	3	3	11	0	0
MRE11A-1	NM_005591	708	7	7	18	0	0
MRE11A-2	NM_005590	680	7	7	17	0	0
MSRB3-1	NM_198080	192	0	0	5	0	0
MSRB3-2	NM_001031679	185	1	1	5	0	0
NBN	NM_002485	754	3	2	15	0	0
NFE2L2-1	NM_006164	605	2	2	4	0	0
NOS2	NM_000625	1153	4	4	25	0	0
PON1	NM_000446	355	4	3	8	0	0
RECQL4	NM_004260	1208	7	6	20	0	0
SERPINA1-1	NM_000295	418	0	0	3	1	0
SMCP	NM_030663	116	0	0	0	0	0
SMUG1	NM_014311	270	5	0	1	0	0
TP53-1,2	NM_000546	393	4	4	9	0	0
	NM_001126112						
WRN	NM_000553	1432	9	8	32	1	2
ZMPSTE24	NM_005857	475	3	3	9	0	0

This table shows quantity of hypermutable CGA codons in each of the listed transcripts. In addition, numbers of such codons which might trigger NMD through PTCs are demonstrated. Zero in this column indicates the failure to elicit "canonic" NMD. Penultimate column shows the occurrence and number of SECIS-like elements, which may prevent protein truncation and NMD elicited by PTCs. Numbers in the last column denote the amount of CGA codons protected by SECIS structures. For additional details, see Online Resource Table S1

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II.5 Relevance for longevity

An engineered suppressor system could be a potential therapy to impact lifespan and age-related diseases. For example, cancer is an underappreciated aging-related disease. Reactivation of tumour suppressor expression due to nonsense suppression would be expected to significantly impact cancer, which would be valuable because cancer is a top cause of mortality worldwide.

Analysis of human gene transcripts reveals that CGA codons are present in aging, DNA repair, and metabolism genes, e.g., APOE, ATM, TP53, and Lamin A (REF).

II.6 Project Status and Future Plans

To date, Dr. Torres and his team have designed and constructed 9 variants of their lead engineered suppressor system. These variants have specific design features that allow for tunability and potentially tissue-specific expression of their system.

At the time of publishing, Artan Bio is finalizing the experimental system to screen the variants. This system will allow us to determine the effectiveness of the various design alterations and select candidates with the desired characteristics. This will be performed in collaboration with a leading CRO.

Once completed, VitaDAO will work with Artan Bio and Dr. Torres to validate the lead constructs in animal models that would serve as the preclinical data to support further development and lead candidate selection. Once positive data has been achieved in the appropriate animal models, Artan Bio will work with CDMOs on scalability and manufacturing to support IND-enabling studies.

From there, clinical studies would commence:

Phase 1 Clinical Trials
Testing of the drug in a small group of healthy volunteers or patients to evaluate safety, dosage, and side effects.

Phase 2 Clinical Trials
Subject to indication selection, Orphan Drug designation could be sought at this stage, which may provide some benefits, including tax credits for certain research and a waiver of the FDA user fee.

Phase 3 Clinical Trials
A trial would be designed to support the registration of a new commercial drug.

FDA Review and Market
Once Phase 3 is complete, a Biologics License Application (BLA) is submitted to the FDA. The FDA then reviews the application, which can take up to 2 years, but may be faster for drugs with a Breakthrough Therapy designation.

II.7 Tokenomics of VITARNA

IP Tokens represent membership in an IP pool containing the IP and R&D data attached to their parent IP-NFT.

The IP Tokens of the ArtanBio IP-NFT are denoted by the token symbol "VITARNA."

The rights of VITARNA token holders are governed by the IPT Membership Agreement.

Token Distribution

A total of 5,000,000 VITARNA tokens will be minted using the Artan Bio IP-NFT.

20% of VITARNA tokens (1,000,000 VITARNA) will be sold to a maximum of 499 participants who are VITA tokenholders, the Governance token of VitaDAO, with the VITARNA tokens purchased in the sale vesting over 12 months with a 1 year cliff.

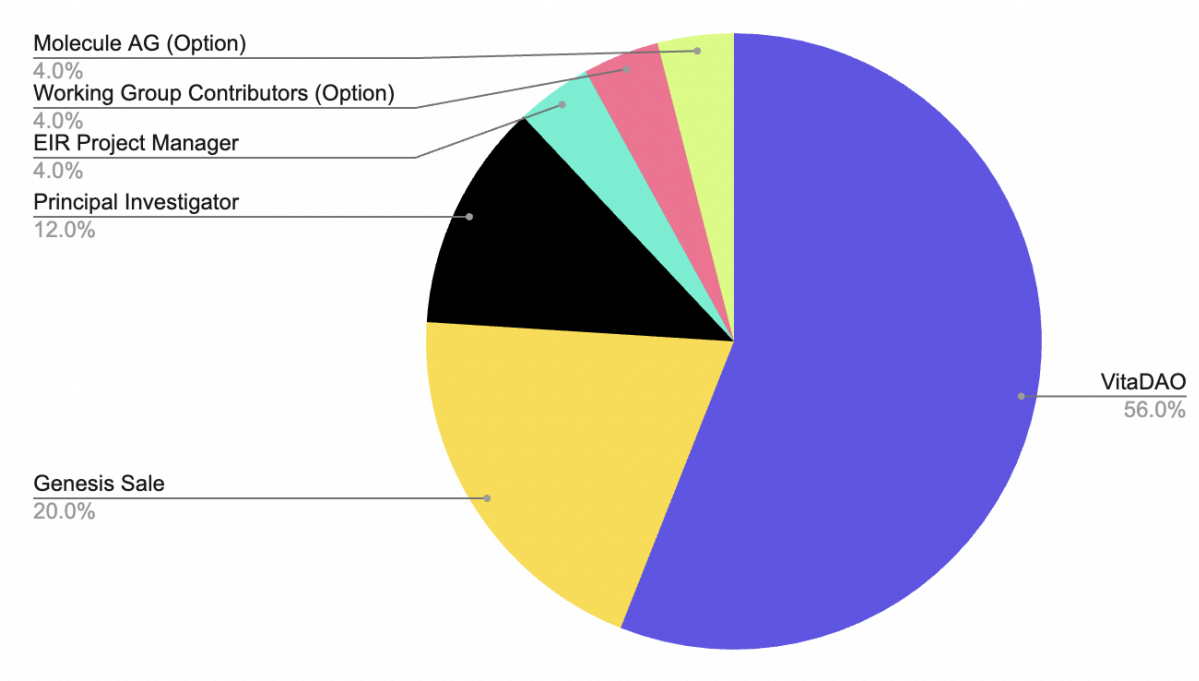
The PI will receive 12% of VITARNA tokens (600 000) vested over 4 years with a 1-year cliff. The vesting period incentivizes long-term success of the project.

VitaDAO's Entrepreneur-in-Residence (EIR) project manager will receive 4% of VITARNA tokens (200 000) vested over 4 years with a 1 year cliff.

VitaDAO's dealflow working group contributors will receive up to 4% of VITARNA tokens (200 000) vested over 4 years with a 1 year cliff. Vesting period incentivizes long-term success of the project, but the distribution must first be approved by VitaDAO governance.

Molecule AG has an option to receive 4% of the VITARNA tokens (200 000) for 10% of the original funding, these tokens will be purchased from VitaDAO.

Assuming the full allocation of tokens to the dealflow working group cited above, and the exercise of Molecule's option to purchase tokens above, VitaDAO will retain 56% of the VITARNA tokens (2 800 000).



II.8 Genesis Sale Structure

The genesis VITARNA token sale will be a fixed-price sale with pro rata distribution, overflow refunds, and 12 month vesting.

20% of VITARNA tokens will be sold to VITA holders at a fixed price determined by an estimated budget of the future funding needs of the project for its next phase as described below.

Needs-based Valuation

The price per VITARNA tokens is determined by a financial needs-based analysis of future activities and does not factor in any appreciation or depreciation in the value of the project, nor the value of the project itself based on the emergent data.

The project team have evaluated the required funding to proceed with the next phase of development and have estimated this to be $300,000 USD. which includes a 10% contingency component as noted below:

II. 9 Proposed Budget

AAV formulation development	$ 15,000.00
In vivo proof of concept studies	$ 150,000.00
AAV preclinical consultant	$ 5,000.00
PI Consultant	$ 25,000.00
IP filing/prosecution	$ 50,000.00
General & Admin	$ 30,000.00
VitaDAO EIR/Management	$ 25,000.00
Total	$ 300,000.00

20% of the IPTs would be issued for this $300,000 USD at a price of 0.30 USD per VITARNA token.

Bidding and Locking (Staking) VITA

The sale of VITARNA tokens will occur over a 14-day period, where members of VitaDAO may bid as much money as they are willing to contribute to the sale.

In order to bid, the bidder must lock (stake) VITA equivalent to the amount of WETH they want to bid. The value of the buyer's bid can be up to the maximum of their VITA holdings locked (staked) in the sales contract. The more VITA a buyer is willing to stake in the sales contract for the 12 month vesting period, the more that buyer may bid during the 14-day sale period. If the sales goal of 79 ETH is not met, all funds will be returned to bidders. Bidders will be required to return to the auction and claim both their funds, and VITA.

Pro Rata Distribution

If the sales goal is met or exceeded, then the final allocation of IPTs will be proportional to each bidder's fraction of the total bids.

For example, if Alice bids 8 WETH and Bob bids 4 WETH, and Alice and Bob are the only funders, then Alice will receive twice the allocation as Bob (this also means that Alice locked (staked) twice as much VITA as Bob).

Overflow Refunds

Any overflow is returned to bidders. If the amount bid exceeds the sales goal, then the excess amount by bidders via the Molecule crowdsale website.

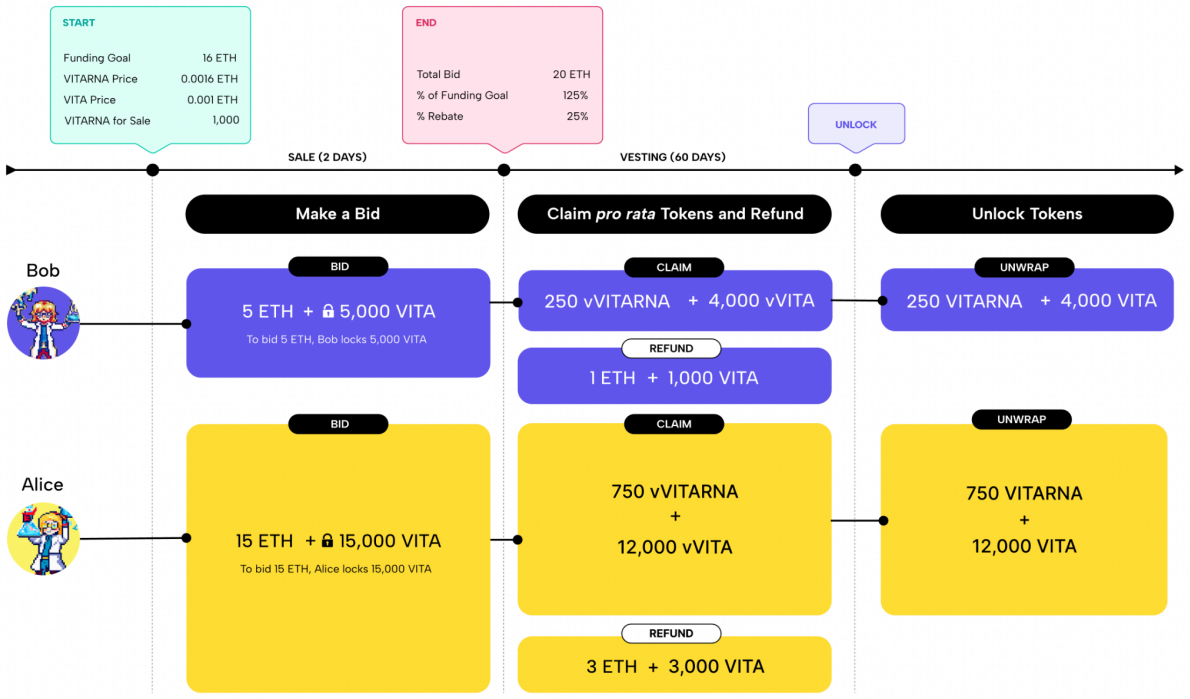
For example, VITARNA tokens sought to raise 79 WETH, but Alice and Bob together bid 80 WETH. The surplus of 1 WETH overflows and is returned pro rata to Alice and Bob, so Alice gets back 0.66667 WETH and Bob gets back 0.33333 WETH.

12-month Vesting

Sale participants receive vested VITA (vVITA) and locked VITARNA (lVITARNA), to ensure they can participate in governance while vesting. After the 12-month vesting period is over, sales participants will be able to swap their vVITA for VITA and lVITARNA for VITARNA tokens. The tokens are locked for the full 12-month vesting period.

VITARNA IPT Crowdsale

Fixed price token sale with pro rata distribution and overflow refunds



II.10 Use of Funds

The immediate application of the funds raised will be to fund the next research steps and to provide access to, and liquidity for, VITARNA tokens. VITARNA holders can decide how these funds will be subsequently used in advancing longevity research and IP development at ArtanBio.

For example, VITARNA holders could vote on the prioritisation of *in vivo* models to pursue. Another example would be voting on conferences to attend to discuss our dataset and promote the strengths of the DeSci and IP-NFT model. A further allocation of funds could be directed towards filing patents. Lastly, holders could vote to enable the generation of additional constructs that address multiple aspects of aging beyond the suppression of nonsense mutations.

In conclusion, while the short-term use of the raised capital will be for ensuring the funding of the next steps in the research as well as preliminary liquidity, through token holder governance, there are various pathways to redirect this capital from liquidity to IP generation. This transition should be a community decision when VITARNA holders have the necessary data and context to facilitate informed decision-making.

Part III: Risk Factors

When purchasing IP Tokens to fund scientific research, several potential risks may apply. It's important to note that this list is not exhaustive and that the specific risks can vary depending on the nature of the project, the research being funded, the structure of the investment, the jurisdiction, and other factors.

Liquidity Risk

The market for trading IPTs might be limited. This could mean you may not be able to resell your IPTs easily or at a price that you find satisfactory.

Regulatory Risk

The regulatory landscape for IPTs and blockchain technology is still evolving. Changes in laws or regulations could have a material impact on the value or legality of your purchase.

Project Risk

The success of the scientific research being funded is not guaranteed. There might be delays, cost overruns, or the research might not yield the expected results.

Technological Risk

As with any digital asset, there is the risk of loss due to hacking, technical glitches, or issues with the underlying blockchain.

Smart Contract Risk

The IPTs are governed by a smart contract and there is a risk that the contract could have bugs or security vulnerabilities that could be exploited.

Market Risk

The value of IPTs could fluctuate due to changes in the broader market for NFTs, biotechnology intellectual property, or cryptocurrencies.

Intellectual Property Risk

There may be disputes or uncertainties regarding the ownership or enforcement of the underlying intellectual property.

Legal & Compliance Risk

Depending on your jurisdiction, owning and trading IPTs or other digital assets might have legal implications, including potential tax liabilities.

Network Risk

The value and function of the IPTs could be impacted by changes or issues with the underlying blockchain network, Ethereum, such as changes in the consensus mechanism, forks, or network congestion.

Operational Risk

The platforms or exchanges used to buy, sell, or store the IPTs could have operational issues, such as downtime, that could impact your ability to manage your purchase.

Governance Risk

IPTs include governance rights and there may be disagreements or disputes among the token holders.

Part IV – Legal and Compliance Considerations

IV.1 – General Conditions Applying to IP Tokens

1. IP Tokens represents membership in an IP pool containing an IP-NFT and its attached IP and R&D data. IP pool membership enables token holders to govern the joint development and experimental use of the IP and R&D data in the pool.
2. IP Token holders may have rights to govern issuance of licences to use the underlying IP and R&D data attached to the IP-NFT. Control over the licensing function of the IP and R&D data is decentralised through token holder governance.
3. IP Token holders may have rights to govern proceeds from licensing or sale of the IP and R&D data. However, distribution of licensing or sale proceeds is not hard-coded. Given regulatory uncertainty, token holders must make a careful judgement in the future about whether, and how, to distribute licensing or sale proceeds, such as by forming a legal entity prior to making such distribution and it is recommended that such decisions include soliciting legal advice.
4. IP Token holders may be granted information rights, entitling them to regular, non-confidential updates from the researchers and the ability to pose queries. This extends to accessing data rooms containing the IP and R&D data, including a continuously open, non-confidential data room. The latter is designed to aid the community's decision-making process through the provision of research results, with proprietary data being redacted to safeguard the IP's integrity. This data room also serves as the primary means for delivering non-confidential updates to holders of IPTs.
5. IP Token holders may also have the opportunity to gain access to confidential data, subject to adherence to protocols such as Know-Your-Customer (KYC) and Non-Disclosure Agreements (NDA) as governed by token holders. This data will be highly confidential, thus requiring users to adhere to such protocols to safeguard the IP.
6. IP Token will not be sold to U.S. or Prohibited Persons. Potential purchasers will be required to provide sufficient proof of their non-U.S. person status including, but not limited to, IP address checks, geofencing, and attestations.

IV.2 – Legality of Purchase

The Issuer and Offerer do not assume responsibility for the lawfulness of the acquisition of IP Tokens by a prospective participant, whether under the laws of the jurisdiction of its incorporation or the jurisdiction in which it operates (if different), or for compliance by that prospective participant with any law, regulation or regulatory policy applicable to it.

Participant's rights may be adversely affected by modifications of the Terms and Conditions that apply to the IP Tokens, as outlined in the associated IPT Membership Agreement, in some cases without their consent when required by law.

IV.3 – Taxation

Each Holder of IP Tokens will assume and be solely responsible for any and all taxes of any jurisdiction or governmental or regulatory authority, including, without limitation, any state or local taxes or other like assessment or charges that may be applicable to any payment to it in respect of the IP Tokens. In the event that any withholding tax or deduction for tax is imposed on IP Tokens, the Holder of the IP Tokens will not be entitled to receive grossed-up amounts to compensate for such withholding tax.

IV.4 – Dependency on Issuer Management

The success of the IP Tokens depends in substantial part on the skill and expertise of the Issuer's management team and the Project team. There can be no assurance that any individual will continue to be affiliated with the Issuer or Project team throughout the lifetime of the IP Tokens or will continue to be available to manage the development program. The unavailability of members of the Project team or Issuer's team to manage the Underlying Assets (IP) could have a material adverse effect on the IP Tokens.

IV.5 – Complaints to Issuer

An IPT Holder may notify VitaDAO of its intention to submit a complaint via the contact information set out in Part I, Paragraph I.1.8, above.

The notification shall be acknowledged within 5 business days, and VitaDAO shall provide information to allow for the intake of the complaint, which shall include a URL which directs the complainant to a website where the complainant may submit their complaint online in the form prescribed by the European Securities and Market Authority[4].

Once received, the complaint shall be transmitted to the IPT Community Representative for the project, and shall be addressed by the Community Representative.

If the complainant is not satisfied with the response or outcome, the complaint shall be escalated to the Coordination Working Group of VitaDAO which may choose to a) seek expert advice and / or b) refer the matter to the IPT Holder membership for resolution or redress.

In the latter case, the Coordination Working Group shall follow the governance procedures of the IPT Membership Agreement and Governance as amended.

[4] Draft – Consultation Paper on the Technical Standards specifying certain requirements of MiCA– Section 9.2.5 – currently in consultation

The IPT Holder shall be bound by the terms of the IPT Membership Agreement both procedurally and with respect to redress.

IV.8 – Recourse to Issuer

VitaDAO, as Issuer, retains the custody of the IP-NFT on which the IPTs are referenced. In the event that VitaDAO should wind down or otherwise be required to cease operations, the IP-NFT referenced by the IPTs shall be transferred from the VitaDAO Treasury to one of a) the project's IPT primary treasury, b) a wallet owned by the research lab or company being funded by IPT proceeds, or c) a purchaser of the IP-NFT. The appropriate option(s) shall be in accordance with the relevant IPT membership agreement (Appendix A) and may be revised by governance by the IPT Holders.

In the event that VitaDAO as Issuer should cease to operate, and according to the provisions noted above, VitaDAO shall only be liable for the transfer of the IP-NFT, and the associated rights and privileges contained therein, in accordance with the IPT Membership Agreement.

IV.9 – Environmental Social and Governance

The Issuer and Offerer rely on the Ethereum blockchain to issue its IP Tokens (IPTs).

The Ethereum Foundation publishes annual reports and includes a review of its environmental impact as part of its environmental, social and governance commitments which can be found here.

Part V: Exhibits and Additional Information

Appendix A – IPT Membership Agreement

VITARNA IPT Membership Agreement

Appendix B – Financial Review

VitaDAO Community Report 2021

VitaDAO Community Report 2022

VitaDAO Treasury Overview

Appendix C – Governance Authorising Issuing of IP Tokens

ArtanBio tokenization proposal (VDP-140)

VitaDAO snapshot proposal approving VDP-140

Appendix D – Other Materials

ArtanBio- VitaDAO Project Page

VITARNA website

VitaDAO Snapshot proposal approving ArtanBio project.

Appendix E – Research References

1. Mort M, Ivanov D, Cooper DN, Chuzhanova NA. A meta-analysis of nonsense mutations causing human genetic disease. Hum Mutat. 2008 Aug;29(8):1037-47. doi: 10.1002/humu.20763. PMID: 18454449.
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