The World's First and Only Safe and Effective Allergy Vaccine for Poison Ivy (PI) & Poison Oak (PO): Investment Opportunity & Business Proposal

(updated 7/20/24)

Wanted: Investors, entrepreneurs, and developers to help commercialize the world's first and only allergy vaccine to safely induce tolerance to PI and (we expect) highly cross-reactive PO

CAPSULE SUMMARY

We unexpectedly discovered/invented/patented the world's first and to-date only proven safe and effective allergy vaccine for PI. Because of their high degree of cross-reactivity it should be equally effective for PO.

We were able to adapt and optimize our formulation and dosing schedule because physicians are allowed to make and modify allergenic products for their own patients without regulatory oversight

On the basis of our human proof-of-concept experience the FDA gave us a no-obstacles pathway to biologics licensure with clinical trials identical to human proof-of-concept experience that was 100% safe and 90-100% effective. We assembled a team of experts and resources

We aren't eligible for NIH SBIR funds because our chemistry team member Prof. Cathy Yang, now works for a for-profit institution where her share of the work would exceed the SBIR limit for a for-profit partner. Hence our solicitation of VC & private investor funding.

The cost of our hand-made human proof-of-concept vaccines, including the professional time of Dr. Coifman and Prof. Yang, was thousands of dollars per course of treatment. Our pre-clinical goal is to validate our strategy fo manufacture GMP vaccine for a cost in the low 10's of $ per initial treatment or annual booster dose, and sell it wholesale for $200.- $300. A commitment of $6M in investor funds before the end of 2024, in return for a 2% ownership share in the company for each $1M of Round 1 investment, will let us complete all pre-clinical work, including preparation of clinical trial vaccine, during 2025.

Commitment of an additional $10M by mid-2025 will let us complete all necessary clinical trials during 2026, for a product launch in 2027. Every $1M of Round 2 investment will buy a1% ownership share in the company.

Between 58 and 116 million Americans meet the clinical indications of having had one severe reaction or unavoidable chronic &/or recurrent exposure and disease. We expect approx..29M of these to want the vaccine as soon as it's validated and available. The company will be profitable from day 1. Reaching 20% of this population by year 5 will generate $1.7B in annual sales of which $1.1 to 1.4B will be profit.

An investment with no regulatory obstacles in which each dollar will pay dividends from launch, by year 5 paying more in annual dividends than the dollar amount of capital investment, sounds too good to be true. Prospective investor(s) can confirm that it isn't by joining us in another pre-IND meeting with the FDA.

A NATIONAL NEED FOR AN EFFECTIVE VACCINE FOR PI/PO

Poison ivy (PI), found east of the Continental Divide, and its highly cross-reactive cousin, poison oak (PO), found west of the Divide, are the most common causes of allergic contact dermatitis in the United States (US). Half of Americans will develop a rash from casual environmental contact at some point and

80-90% will become clinically sensitized with higher levels of exposure (1). In a 2006 general review of Toxicodendron dermatitis (2) Gladman points out that even 20% of Americans living in urban environments experience clinical allergic contact dermatitis from PO/PI, that allergy to PO/PI causes 10% of all US Forest Service lost-time injuries, and that approximately one third of forestry workers in California, Oregon, and Washington are disabled by poison oak dermatitis each season. During severe fire seasons in the western United States up to 25% of U. S. Forest Service firefighters must be removed from duty because of this condition (3). In the late 1990's the cost of treating occupational allergic contact dermatitis from PO/PI consumed 1% of the State of California's entire yearly workers' compensation budget (4).

COMMERCIAL GOAL

To bring to market the world's first allergy vaccine for the urushiols of poison ivy (PI) and poison oak (PO) that is both safe and effective at a low enough cost of production to achieve all of user availability, user and payer affordability, and developer profitability.

THE PRODUCT

The product will be a 100 mg / ml concentrated crude ethanol extract of PI cloned from genetically selected plants in the same field from which we made our safe and effective human proof-of-concept series vaccines. It will be packaged and stored under conditions shown in shelf-life stability studies to optimize shelf life at minimum cost.

VACCINE DEVELOPMENT TEAM

- **Robert Coifman MD** is BOME Pharma CEO, chief science officer, and PI/PO vaccine development program principal investigator. He is an allergist in solo practice in Millville NJ, an engineer by pre-medical training and orientation. He will provide scientific and medical direction and leads outreach to potential investors.
- **Eric Feerst** is project manager and a retired NJ DEP lab chief. He will perform Prof. John Jelesko's seed germination protocol and oversee both process quality control and regulatory affairs.
- **Merlin Weaver** is a hydroponic vegetable farmer on whose farm the PI/PO cultivation greenhouse will be erected and by whose staff it will be serviced. Merlin will apply standard commercial scale agricultural methods to the cultivation of PI and PO, and his staff will provide greenhouse maintenance services.
- **Catherine Yang PhD**, our chemistry partner and co-inventor of our PI/PO vaccine, is currently Vice President of Academic Affairs and Associate Dean of Medical Education at California Northstate University. She will oversee urushiol assays on samples shipped to her in CA.
- **Millan Bhatt** is managing partner of the Molecular Pharma Group, a USP 503b sterile compounding pharmacy in New Providence, NJ. He will perform GMP desiccated vial filling and packaging.
- **Mel Kornbluh** is a serial developer of successful small businesses dependent on various forms of efficient precision technology. He was instrumental in assembling the vaccine development team and will continue to work with us as a consultant and potential provider of sales and distribution services.
- **Scott Oneto** is a University of California Cooperative Extension Farm Advisor and the senior weed scientist at the University of California at Davis College of Agriculture. He was instrumental in the assembly of our cultivation technology protocols and will continue to serve the project as a consultant.

THE COMPANY

We established a NJ limited liability company, BOME Pharma LLC, as the entity that will ultimately commercialize the vaccine. Up to this time, to minimize overhead and because of evolution in the roles of the various team members while the project remains mostly dormant but ready to roll, it's been most practical for us to work as an informal network of the individuals named in our accompanying science proposal.

The company will be converted to a C-corporation when it receives investor funding and commences activity as a business. It will form a subsidiary, BOME Agra, to qualify for the NJ agricultural business sales tax exemption and to set up and operate facilities for the cultivation of crops and the drying of freshly harvested leaves.

U.S. MARKET ANALYSIS

We present 4 separate estimates of the # of persons in the U.S. likely to want the vaccine based on different assumptions regarding two different data sets.

The first two estimates are based on the widely quoted citation that 10 to 50 million Americans seek medical care each year for allergic contact dermatitis from PI or PO. This range is cited in the medical reference website UpToDate's review of Poison ivy (Toxicodendron) dermatitis (5), updated 10/16/2023, reports that 10 to 50 million Americans need medical treatment for allergic contact dermatitis to PI or PO every year. Source-tracing leads to a report published in 2003 (6), that appears to have been written for the lay public. It states that “Each year 10 to 50 million Americans develop an allergic rash after contact with these poisonous plants” (PI and PO) but it cites no data and gives no source. The same estimate of 10 to 50 million cases per year is quoted by a public information website (7) and by the most authoritative recent scientific review (8).

CDC national health survey data reviewed by journalist Sammy Fretwell reported a 7% annual increase in number of US ER visits for PI and PO from 2002 to 2012 (9). The factors responsible for this increase, climate change, suburbanization and population growth, persist unchanged. As patients seeking ER care for allergy to PO or PI are the most severe cases who are candidates for our vaccine to avoid recurrence we believe the 7% annual increase in emergency department visits is probably a reasonable measure of the annual rate of increase in the number of patients identified as being severe allergic and likely to want a vaccine that will prevent recurrence on repeat exposure.

For this mathematical model we will assume that the minimum number of estimated annual cases is a reasonable estimate of the number of cases severe enough to qualify for and want the vaccine. The most recent annual utilization data that could have been reported in 2003 would have to have been for 2002. App-lying the 7% rate of annual increase, a vaccine candidate population of 10M highly allergic individuals who have severe enough reactions to require emergency department care and want a vaccine to prevent recurrence, grows to 57.5M vaccine candidates in our earliest possible market year, 2027.

Our second estimate is based on the question of whether the documented 10-year 7% annual increase in annual # of U. S. emergency department admissions for PO/PI includes enough one time cases of only moderate severity to be an overestimate of the actual annual increase in the number of identified severely allergic individuals for whom the vaccine is not only indicated but the patient should also be motivated. We therefore made a parallel estimate of the annual number of vaccine candidates based on an annual increase of 5% instead of 7%, from the same starting point of 10M ER visits in 2002. This yields an estimate of approx. 35M highly allergic Americans wanting a safe and effective vaccine to prevent recurrence.

An alternate calculation can be based on prevalence reports of clinical allergy of varying degrees of severity to PI and PO. In 1996, Epstein & Epstein reported a prevalence of clinical allergy to PO/PI of 50% of the U. S. population (1). In 2019, after 20 years of climate change and increasing suburbanization, Kim et al reported the same prevalence as 50-75%. Neither cites supporting data though Epstein had performed numerous population studies of the spectrum of sensitivity. In 1994 Epstein split his population analysis into 1/6 (16.7%) clinically very sensitive, 1/3 (33.3%) clinically moderately sensitive, 5/12 (41.7%) subclinically sensitive (ho history of symptoms but will react to a sufficient challenge) and 1/12 (8.3%) totally tolerant (4).

To estimate the fraction of genetically very sensitive persons who have already had an episode of disease and want a vaccine to prevent recurrence we can assume that the risk of sufficient exposure to provoke a reaction is constant throughout life. Under that assumption, at any point in time approx. 50% of

genetically very sensitive persons will have already had an episode of illness for which their severity, as very sensitive persons, will make them want a vaccine to prevent recurrence. That the actual fraction of the very sensitive population who have already had an episode and want the protection of our vaccine is actually greater than 50% is suggested by Epstein's finding (4) of a predisposition of sensitive individuals to experience clinical disease before reaching adulthood. Very sensitive individuals are also more likely that those who are less sensitive to have encountered triggering doses earlier in life than those who are less sensitive because a larger fraction of the spectrum of exposures we all encounter as we go about life are above their triggering threshold and will have triggered reactions. We can't attach numbers these demand-increasing factors so we'll base our numerical demand projection on the assumption that the average risk of an index exposure is constant throughout life and that when the vaccine is approved for sale approx. 50% of the very sensitive 1/6 of the population will have had at least one severe reaction, know that they're very sensitive, and will want a safe and effective vaccine. Because more than 50% of the genetically very sensitive fraction of the U. S. population will in fact have had a reaction they'll want the vaccine to prevent having to repeat, real market demand is likely to exceed our calculated market projections of 28.9M very sensitive Americans knowing from past experience that they're very sensitive and wanting our vaccine if it becomes available in 2027.

There are mildly and moderately sensitive persons who will want the vaccine because of chronic or recurrent exposure they find it impractical to avoid. Suburbanization, increasingly outdoor life styles and the effects of climate change will increase the fraction of the 113M (1/3 of the U. S. population) who are mildly or moderately sensitive who will have chronic or recurrent exposure and reactions and also want the vaccine. Their number may possibly equal or exceed that of the very sensitive vaccine candidates. They will also want the vaccine more urgently than past severe reactors who are not currently having symptoms as they want relief NOW while past severe reactors are like candidates for vaccines for shingles, considering a vaccine to prevent something unpleasant that may otherwise happen at some point in the future. We chose to calculate a 4th model of vaccine demand assuming that 5% of the 113M Americans who are moderately sensitive to PO or PI will have sufficient chronic or recurrent symptoms to also want the vaccine as soon as it's available, yielding an estimated 2027 target market of 34.7M.

Total market estimates (total number of Americans who will be vaccine candidates) are listed for each of these 4 market projection models for each of years 2027-31in the 4 market estimate lines at the top of Table 1. Estimates #2 and 4, derived from different analyses of different data sets, are roughly similar across the 5-year time span. However, to keep our income projections on the conservative side we will base income and profit calculations on the most conservative projection of market for the vaccine, only the conservatively estimated 50% of very sensitive patients we're protecting to have had an index reaction and know that they're very sensitive and therefore want the vaccine.

For the economic projections in the lower part of Table 1 we chose the most conservative of the four market projections discussed under U. S. Market Analysis, the estimate of 28.9M consisting of the minimum estimate of 50% of the very sensitive population who will have had one or more sufficiently severe reactions to want a vaccine to prevent recurrence. The table shows revenue and profit projections based on manufacturing costs for each initial treatment or annual booster dose of $30, $60 and $120 and wholesale selling prices of $200, $300 and $400. With anticipated end user or insurer costs approximating twice our wholesale selling price we've tried to estimate the impact of end-use payer cost and insurance coverage on market demand. Insurers may determine, for example, that at an annual vaccine cost of $800 they may minimize the sum of their total costs of prevention (with the vaccine) and treatment (of patients who don't get the vaccine) by automatically approving coverage for patients with two or more documented episodes and forcing those with a single episode for which they want protection against recurrence to go through the pre-authorization process. Or, they may impose copays forcing patients to choose between risk of recurrence and cost of protection.

We chose to accommodate these variables in the table by estimating that if we sell the vaccine at a wholesale price of $200, in year 1, one of every 64 people in our target population of 28.9M Americans will get the vaccine and begin annual boosters, that this fraction will double every year through year 5 at which it will reach 25%. If, instead, we charge a wholesale price of $300 with an anticipated final payer

cost of $600, we are estimating that we'll lose 20% of this market, with an initial year market penetration of 1 of every 80 doubling every year to a year 5 market penetration of 20%. We estimated that if we increase our wholesale selling price to $400, resulting in an annual final payer cost of $800 per patient per year, we may lose up to half of the market we'd have at a wholesale selling price of $300, with a year 1 market penetration of 1/160 doubling every year to a year 5 market penetration of 10%.

In the tables for each of our low, medium and high production and sales cost calculations the market size is the number in the box at the top of the table for our most conservative demand model, of only the 50% of very sensitive patients conservatively estimated to know that they're very sensitive and want the vaccine. The net line, "Mkt $", is the total size of the market in dollars at our selling price for that cost & selling price model. None of these economic projections include estimates of demand from mildly and moderately sensitive persons with unavoidable chronic or recurrent exposure and disease. They will not only boost total demand but also jump-start early demand because they want protection from symptoms that are there NOW and not just protection from events that may recur at some point in the future.

Professional market estimators can determine if my estimates of market penetration as a function of wholesale selling price are accurate but they illustrate the price optimization process. If my market penetration estimates as a function of wholesale selling price are accurate it will serve our interest to sell the vaccine at a wholesale price of $300 no matter what our actual production cost within the projected range of $30 to $120 per initial treatment dose or annual booster. Depending on manufacturing cost within this range projected year 1 profit from the very allergic population alone will be $65-98M and year 5 profit will be $1.1-1.6B.

Table 1, Market Projections

	2027	2028	2029	2030	2031
Market estimates based on minimum est 2002 utiization rdata 7/% annual growth					
	57546027	61718584	66193687	70993271	76140864
Market estimates based on minimum est 2002 utiization rdata 5/% annual growth					
	34903430	36692967	38574255	40552000	42631145
Market est. 50% of those severely allergic will have had a Sv reaction = 1/12 of projected US pop					
	28924855	***29067071***	***29207778***	***29346858***	***29483581***
+ est 5% of mild-moderate unable to avoid = 10% addition to # seveely allergic c/pos Hx					
	34709826	34880485	35049333	35216230	35380297

Base yr		2027	3 cost/sell models	Low	Mid	High
Growth / yr		7%	Cost to mfr	$30	$60	$120
Mkt size #		7838102	Sell at	$200	$300	$400
			2027	2028	2029	2030	2031
Market share & $$ goals for:			2027	2028	2029	2030	2031
Market #			28924855	29067071	29207778	29346858	29483581
Mkt $ Low	c$30 s$200		$5,784,971,017	$5,813,414,150	$5,841,555,533	$5,869,371,683	$5,896,716,233
Target Fx			1/64	1/32	1/16	1/8	1/4
Target sales			$90,390,172	$181,669,192	$365,097,221	$733,671,460	$1,474,179,058
	less cost		-$13,558,526	-$27,250,379	-$54,764,583	-$110,050,719	-$221,126,859
	profit		$76,831,646	$154,418,813	$310,332,638	$623,620,741	$1,253,052,200
Market #			28924855	29067071	29207778	29346858	29483581
Mkt $ Med	c$60 s$300		$8,677,456,525	$8,720,121,225	$8,762,333,300	$8,804,057,525	$8,845,074,350
Target Fx			1/80	1/40	1/20	1/10	1/5
Target sales			$108,468,207	$218,003,031	$438,116,665	$880,405,753	$1,769,014,870
	less cost		-$21,693,641	-$43,600,606	-$87,623,333	-$176,081,150	-$353,802,974
	profit		$86,774,565	$174,402,425	$350,493,332	$704,324,602	$1,415,211,896
Market #			28924855	29067071	29207778	29346858	29483581
Mkt $ High	c120 s400		$11,569,942,033	$11,626,828,300	$11,683,111,067	$11,738,743,367	$11,793,432,467
Target Fx			1/160	1/80	1/40	1/20	1/10
Target sales			$72,312,138	$145,335,354	$292,077,777	$586,937,168	$1,179,343,247
	less cost		-$21,693,641	-$43,600,606	-$87,623,333	-$176,081,150	-$353,802,974
	profit		$50,618,496	$101,734,748	$204,454,444	$410,856,018	$825,540,273

THE CUSTOMER

If the FDA lets pharmacists supervise vaccine administration as they do for COVID and flu vaccines, our largest volume customers will probably be pharmacy chains, followed by drug distributors. Wholesale and retail distributors will be our major customers if administration is restricted to licensed prescribers. Allergenic products that are further restricted “for use by physicians who are experienced in the administration of allergenic extracts," and require a different supply chain are those that carry a risk of systemic anaphylaxis. That is not a risk of our vaccine.

FDA RETAIL APPROVAL

The FDA will allow administration under supervision by pharmacists if clinical trial adverse effects requiring acute physician care are rare to non-existent. We can control the frequency and severity of adverse effects with our choice of vaccine starting dose and dosing schedule. We can reduce adverse effect frequency and severity with a lower starting dose and a slower dosing schedule with a larger number of steps. We believe we can keep the side effect profile sufficiently benign to allow administration in retail pharmacies with a 6-step dosing schedule for Phase 1 dose-ranging recipients of a cumulative 15 mg dose, 7 steps for recipients of a cumulative 25 mg dose, and 8 steps for those receiving a cumulative treatment dose of 35 mg. **We plan to offer free access to a national dose-tracking database, so that a patient can get one dose at a Walmart in Maine and the next scheduled dose at a CVS in Los Angeles.**

COMPETITION

A poison ivy vaccine developed by Hapten Sciences LLC was registered at ClinicalTrials.gov to enroll patients beginning in April 2021 with an estimated completion date of 12/1/22. However, the sponsors have posted no status updates since August 2021.

The vaccine to be studied was a water-soluble urushiol acetate ester that the company’s scientific founder, Dr. Mahmoud ElSohly, has been studying at the University of Mississippi since the 1970's. It does not precipitate in its target tissue like our water-insoluble urushiol vaccine, and it had not previously been studied in humans. Dr. ElSohly’s published scientific data and the fine print on the Hapten Sciences website indicate a HOPE (with no confirming evidence) that their vaccine MAY induce tolerance if given to genetically susceptible persons BEFORE they’re exposed and sensitized to PI or PO. **We do not see this vaccine as a serious competitor to our vaccine with its proven record of safe and effective induction of tolerance in persons who are already allergic.**

THE SPREAD OF PI/PO ALLERGY & GLOBAL MARKET POTENTIAL

PI and PO evolved in North America. Related Toxicodendron species exist in enclaves in South America. The Chinese / Japanese lacquer tree is a member of the family that crossed the former land bridge between Alaska and Asia. Other trees of the Anacardiaceae family produce urushiols that can cross-react, including mango, poison sumac, Peruvian pepper, pistachio, and cashew. The urushiol content is usually higher in the skin or shell than in the flesh of the fruit. Cashews are typically sold shelled (to eliminate most of their urushiol) and roasted (to degrade what remains). Urushiol-allergic persons with occupational exposure to these non-PI or PO urushiols are potential candidates for the vaccines of the present project. PI and PO are slowly spreading world-wide, from seeds transported in global commerce.

INTELLECTUAL PROPERTY (IP) PROTECTION

Drs. Coifman and Yang’s US Patent 9,107,901 for VDBP for the urushiols of PI, PO and related plants, expires in 2030 (10). They have broader patents for VDBP in Great Britain, Germany and India. A provisional patent application is currently in preparation for Prof. Yang’s low cost urushiol assay. Having exclusive access to an assay that costs $25 when the assay cost for potential competitors is `$800 will give us a functional monopoly on vaccine production until 2044.

FINANCE OPTIONS

Option A, Partial Ownership Investment Opportunity

We will need $4-6M to complete the two pre-clinical projects scheduled for calendar year 2025 if we have the necessary investor funding in time. These are the conduct of shelf-life stability studies and the population of a cultivation greenhouse with enough clones of vines selected for homogeneity of their genetically determined congener production patterns to produce enough vaccine for clinical trials by the end of the year.

An additional $8-10M in investments, if received by the end of 2025, will allow us to conduct clinical trials in 2026, which we expect to be successful as both the vaccine to be used and the subjects to be immunized will be essentially identical to those yielding 100% safety and 90-100% efficacy in our published human proof-of-concept experience. We expect this investment to carry us through launch from which point we expect commercial operations to be profitable because of the tens of millions of Americans eager to receive a safe and effective PO/PI allergy vaccine as soon as it's validated and available.

Option B, Total Ownership Investment Opportunity for a Manufacturer Purchaser

Candidate investors for total ownership are established pharmaceutical or vaccine manufacturers with in-house capability to manage vaccine development and also marketing, sales and distribution for administration in retail pharmacies.

1. A qualified total ownership manufacturer purchaser will have the option to contract with us for our team to perform whatever components of vaccine development it wishes to hire us to do and/or to consult as it chooses if it elects to have the vaccine development work done elsewhere. We suggest that our team in our facilities will be the most cost-effective provider of a quality product.

2. A manufacturer purchaser will pay $3M to BOME Pharma LLC for work previously done, plus a royalty of 50% to be added to whatever selling price it would like to receive for itself at the last point in the supply chain from manufacturer to recipient that the vaccine is sold by an entity with shared or overlapping ownership with the manufacturer purchaser.
    a. The royalty will apply for the life of the product, but its percentage may be renegotiated, if there is mutual agreement to do so, in the event that an equally safe and effective competing vaccine with no shared or overlapping ownership ever appears in the market and creates true price-based competition.
    b. In the absence of price competition by an independently owned equally safe and effective vaccine, we do not see this royalty on top of a price giving a manufacturer purchaser a reasonable return on its investment as having a significant adverse impact on sales or revenue for the manufacturer purchaser. We see this as a reasonable way for a manufacturer purchaser to pay us on the basis of the actual revenue it generates with our vaccine.

3. We need to be protected against the possibility that a large manufacturer purchaser may want to purchase our vaccine but then set its development aside to focus on other products. This protection will have two components:
    a. The manufacturer purchaser will pay BOME Pharma LLC a minimum of $1.5M at the beginning of each 12-month period for 20 years from the signing of a purchase agreement. This will be an advance against future royalties at any time during this interval that it is not covered by actual royalties earned.
    b. If the vaccine has not entered clinical trials within 5 years from the date of signing or achieved biologics licensure within 8 years from date of signing, BOME Pharma LLC or any successor entity will have the option to reclaim the vaccine for a price of one dollar,

with no obligation to repay either manufacturer purchaser's advances against future royalties or manufacturer payment for prior work.

Hybrid finance option C for a manufacturer: Partial ownership investment with opportunity to purchase outright:
The investment value of our vaccine development project depends on the accuracy of our claims about the pathway to licensure given to us by the FDA. When a serious investor or consortium or investors are otherwise ready to commit, we'll be happy to request another pre-IND meeting with the FDA in which they can participate and for which they can submit questions. The FDA will probably let us do this only once, so we must reserve this opportunity for an investor, group of investors or potential manufacturer purchaser that is otherwise ready to sign on the dotted line.

CLINICAL TRIAL ORGANIZATION & MANAGEMENT

Outreach to a sampling of Clinical Research Organizations (CROs) that manage clinical trials for vaccines found none interested in working with a PI/PO allergy vaccine. One VC company that operates a CRO business and invests in biopharmaceutical developers for which it conducts clinical trials expressed interest in working with us and asked us to contact them when we are ready to begin clinical trial design.

If we cannot find a CRO, it should be possible to put together a clinical trial network of allergists who already have clinical trial businesses and to arrange for administration and data analysis that meets the FDA's requirement for freedom from conflict-of-interest through one of the national allergy specialty societies.

CLINICAL TRIAL DETAILS (AS CURRENTLY PLANNED)

FDA Phase 1: The fastest path through Phase 1 will be to concurrently treat 10 subjects exposed and allergic to PI with each of 15, possibly 20, 25 and 35 mg of PI vaccine at one of a small number of centers in the eastern U.S. where the predominant source of urushiol causing human sensitization and illness is PI.

To accommodate an up to 50% drop-out rate without loss of study validity, we will budget for 20 subjects to receive each of up to 4 different study doses. Each set of patch tests will take 2 to 4 visits. The average Phase 1 course of treatment will take 7 steps, but we will budget for 8 to accommodate any schedule adjustments that might be necessary.

We are not budgeting direct costs for any non-responders who request a booster dose, but we plan to offer that option and pay for it as an indirect cost.

Future Phase 1 Testing to Extend Vaccine Use Life: Our timeline to achieve the earliest possible product launch date will necessarily require us to use a vaccine less than 1 year old for both Phase 1 and pivotal Phase 2 clinical trials. We hope to be able to negotiate for a standard protocol with which we can test the response of small groups of subjects with progressively older lots of vaccine and use those results to request extension of use life for both new and existing lots of the vaccine.

Phase 2 Pivotal Clinical Trials: Phase 2 pivotal clinical trials will test and treat 30 subjects each (or any higher number required by the FDA) who are exposed and allergic to PI (in study centers east of the Continental Divide) and exposed and allergic to PO (the predominant source of human urushiol exposure in the drier climate of the West).

We will budget for 3 quarterly follow-up questionnaires, though probably combine the final one with 12-month follow-up for repeat patch testing. An incentive for subjects to return for f/u patch testing will be a free booster dose. Booster doses will initially be given in a single step but switch to 2 steps if single step boosters turn out to have a significant frequency of reactions.

Phase 1 clinical trial subjects who were randomized to the cumulative vaccine dose subsequently selected for Phase 2 use will be added to the follow-up cohort. As in Phase 1 we will offer booster doses to any Interested Phase 2 clinical trial subject with an unsatisfactory response to initial treatment. Also, as in Phase 1, these will be budgeted as indirect costs.

Possibility of NIH SBIR Clinical Trial Funding: We did not qualify for NIH SBIR pre-clinical funding because team member Prof. Catherine Yang's employment by a for-profit institution would classify her share of project work in a category that exceed the limits of the SBIR program.

Once a clinical trial vaccine has been made, this division of work will no longer apply, and we'll be eligible for NIAID SBIR clinical trial support if we remain a US-owned SBA-defined small business that is not majority-owned by private equity and that employs its principal investigator at least 50% of full time.

Clinical Trials to Support Annual Booster Dosing Schedule:
All Phase 2 clinical trial responders and all Phase 1 responders randomized to the treatment dose subsequently selected for Phase 2 will be invited to receive boosters one year after initial treatment. Boosters will initially be given in a single step but switched to a 2-step schedule if single step dosing is associated with a significant frequency of uncomfortable reactions. We think it extremely unlikely to have to go to a 3-step booster schedule.

Clinical Trial Costs: Projected direct costs of the above clinical trials are tabulated in Table 2 on the next page. Indirect costs including costs of IRB, any study-related clinical care of subjects, data collection and analysis and communication with the FDA may total up to 5-6x direct costs bringing the projected total cost of clinical trials to approx. $7M.

Table 2, Projected Clinical Trial Direct Costs Costs

	n	#	$	tot	What
Phase 1 dose ranging					
	Pre-patch #1, 2-4 visits				
	80	4	$150.00	$48,000.00	Center pmt
	80	4	$50.00	$16,000.00	Subject honorarium
	Pre-patch #2, 2-4 visits				
	80	4	$150.00	$48,000.00	Center pmt
	80	4	$50.00	$16,000.00	Subject honorarium
	Tx max 8 visits				
	80	8	$150.00	$96,000.00	Center pmt
	80	8	$50.00	$32,000.00	Subject honorarium
	Post patch 2-4 visits				
	80	4	$150.00	$48,000.00	Center pmt
	80	4	$50.00	$16,000.00	Subject honorarium
$320,000.00	***Direct cost subtotal***				
Phase 2 PI + PO combined					
	Pre-patch #1, 2-4 visits				
	120	4	$150.00	$72,000.00	Center pmt
	120	4	$50.00	$24,000.00	Subject honorarium
	Pre-patch #2, 2-4 visits				
	120	4	$150.00	$72,000.00	Center pmt
	120	4	$50.00	$24,000.00	Subject honorarium
	Tx max 8 visits				
	120	8	$150.00	$144,000.00	Center pmt
	120	8	$50.00	$48,000.00	Subject honorarium
	Post patch 2-4 visits				
	120	4	$150.00	$72,000.00	Center pmt
	120	4	$50.00	$24,000.00	Subject honorarium
$480,000.00	***Direct cost subtotal***				
	Quarerly F/U s/ visit # 3 for all Phase 2 + Phase 1 given dose selected for Phase 2				
	140	3	$50.00	$21,000.00	Subject honorarium
$21,000.00	***Direct cost subtotal***				
	12 mp f/u c/ rpt patch testing, , 2-4 visits				
	140	4	$150.00	$84,000.00	Center pmt
	140	4	$50.00	$28,000.00	Subject honorarium
	Booster dose initially 1 step but may need to split into 2 if 1 => reactions				
	140	2	$150.00	$42,000.00	Center pmt
	140	2	$50.00	$14,000.00	Subject honorarium
	Post booster patch test, 2-5 visits				
	140	4	$150.00	$84,000.00	Center pmt
	140	4	$50.00	$28,000.00	Subject honorarium
$280,000.00	***Direct cost subtotal***				
$1,101,000.00	***Direct cost total***			***$1,101,000.00***	
Ea add'l Phase 1 for use life extension		(Need 10 recruit 20,sunke pre-Tx only))			
	Pre-patch #2, 2-4 visits				
	20	4	$150.00	$12,000.00	Center pmt
	20	4	$50.00	$4,000.00	Subject honorarium
	Tx max 8 visits				
	20	8	$150.00	$24,000.00	Center pmt
	20	8	$50.00	$8,000.00	Subject honorarium
	Post patch 2-4 visits				
	20	4	$150.00	$12,000.00	Center pmt
	20	4	$50.00	$4,000.00	Subject honorarium
$64,000.00	***Direct cost subtotal***				

COSTS OF BLA APPLICATION AND LAUNCH

Allergenic products are exempt from the otherwise applicable fee of $3,117,218. We were unable to get a specific dollar cost for CBER's Managed Review Process but understand that it is in the range of $1-2M.

For launch we'll be able to draw on the sales and distribution resources of team member Mel Kornbluh's other business, Vineland Syrup. Inc., at which project manager Eric Feerst already manages sterile product regulatory affairs with the FDA. We estimate total costs from clinical trial to BLA and launch should not exceed approx. $10M.

PRODUCTION

Details of our planned commercial production strategy are spelled out in our accompanying Science Proposal. The significant business aspect is that we expect to be able to make it at a cost of approx. $30 per initial treatment dose of annual booster and sell it at a wholesale price of $200 - $300 at which prices tens of millions of Americans are expected to want it. Treatment with the vaccine will be less expensive than medical care of the same population without it, which will motivate insurers to not only cover it but also to promote it for their at-risk insureds.

MARKETING EFFORTS

A marketing strategy will depend largely on who our customer is, as discussed above. Marketing will include efforts to generate positive media exposure as the vaccine approaches its launch date for commercial sale. We expect media publicity of vaccine availability and advertisement by pharmacies to use vaccine availability as incentive to bring customers to their stores to make other purchases will generate enough interest among the 36M Americans we estimate to be vaccine seekers in launch year 1 to generate enough revenue to support whatever additional marketing the Board and advisors deem worthwhile.

REVENUE STREAM

Revenue will come from sales of our vaccine, for which between 58 and 116M Americans either do now or in the future will meet clinical indications. Of these, we believe the projected 29M seeking medical care for PI or PO in our earliest projected launch year of 2027 and 48 million in our earliest projected sales year 5 in 2033 are reasonable estimates of the number who both meet clinical indications and are likely to actually want a safe, effective, affordable and conveniently available vaccine.

COST & SALE PROJECTION RANGES

High Cost and Sale Projection – mfr each unit for $120, sell wholesale for $400, end user or payer cost of $800: Every one of the nearly 29M patients in our 2027 target market population will be very sensitive to PI or PO and will have already had at least one severe reaction and should want a safe and effective vaccine to prevent recurrence. If the end user cost to insurers is twice our wholesale selling price it's possible that insurers might calculate costs and conclude that it would cost them less to treat recurrent episodes in those patients in this group with less frequent exposure or less severe reactions than to vaccinate them at a cost of $800 per year.

While we hope this doesn't occur, it's been built into this economic analysis by presuming that if we sell vaccine at a wholesale unit price of $200 (1 unit = 1 initial course of treatment or annual booster) by market year 5, we'll reach 25% of our target market while at a price of $300 we'll reach 20% and at $400 only 10%.

While this doesn't account for moderately sensitive patients with chronic or recurrent exposure into our demand prediction (because we do not know how numerous these patients are), we can assume they are plentiful as they comprised a majority of those who managed to find us and request treatment during our human proof-of-concept series. It will be hard for insurers to justify denying access to the vaccine for them

as their illness and need for care will be chronic and almost certainly cost more per year than the vaccine at annual cost of $800.

Mid-range Cost and Sale Projection – mfr each unit for $60, sell wholesale for $300, end user or payer cost of $600: In this example, we assume a market penetration of 20% by market year 5. As for both the high and low-cost calculations, we back-calculated sales for years 1-4 so that sales would double every year until reaching the year 5 market fraction chosen for this example.

Low cost and sale projection: mfr each unit for $30, sell wholesale for $200, end user or payer cost of $400: This scenario uses a year 5 market penetration of 25%. What this computational exercise teaches us is that if we could confirm that the market vs wholesale selling price relationship chosen for this example could be predicted for the real business world, the company would be most profitable if it sells the vaccine at a wholesale price of $300 per unit no matter where within the range of this example our manufacturing price actually turns out to be.

INVESTOR OPPORTUNITY TO VALIDATE CLAIMS WITH THE FDA

The investment value of our vaccine development project depends on the accuracy of our claims about the pathway to licensure given to us by the FDA. When a serious investor or consortium or investors are otherwise ready to commit, we'll be happy to request another pre-IND meeting with the FDA in which they can participate and for which they can submit questions. The FDA will likely permit us to do this once, so we must reserve this opportunity for an investor, group of investors or potential manufacturer purchaser that is otherwise ready to sign on the dotted line.

We thank you for your interest in becoming a partial owner of this vaccine as an investor. We'll be happy to address any and all questions, scientific, regulatory, economic, procedural or other.

Robert E. Coifman, M.D.

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