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

(updated 10/27/24)

Wanted: Investors 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

The Food Drug and Cosmetic act allows an individual physician to make allergenic products for his own patients without regulatory oversight. Previously licensed vaccines for PI and PO, which impressed me as offering moderate partial relief to many severely allergic patients, were pulled from the U. S. market in 1994when allergenic products for the first time had to demonstrate efficacy as well as safety and no manufacturer submitted efficacy data to the FDA. When a severely allergic professional tree trimmer came to me for care a number of years ago, after obtaining informed consent I collaborated with chemistry partner Prof. Catherine Yang to make a vaccine for him from locally growing leaves. To make it practical to make a safe small lot of vaccine without a sterile fabrication facility we chose to dissolve the urushiol in ethanol instead of sterile vegetable oils. We injected it into muscle instead of under the skin so the small injected volume of ethanol, which is a tissue irritant, would be rapidly diluted to non-irritating concentrations by the water content of skeletal muscle.

We expected to achieve a moderate reduction in our patient's daily need for prednisone. We were pleasantly surprised to achieve the world's first induction of complete immunological tolerance in a person previously sensitized to PI. We then offered the same treatment to others, modifying our formulation and dosing schedule based on accumulating experience, until we achieved a dose and formulation achieving measurable and durable real world tolerance in 90% of treated patients, with a 100% response of patients with a sub-optimal initial response to a single booster dose, and no significant adverse effects of treatment. We patented the vaccine, tried to figure out the science of what we'd discovered, and put together a team to make a formulation compatible with FDA requirements at a cost-effective commercial scale.

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 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 to manufacture GMP vaccine for a cost per initial course of treatment or annual booster in the range of ~$30 and sell it at a wholesale price of ~$300 as the only safe and totally effective treatment option for the tens of millions of Americans with either one or more episodes of severe allergy or chronic or recurrent exposure triggering mild or moderate allergy. We are seeking Round 1 funding from personal contacts and a nationwide database of physicians in the specialties most familiar with both the medical need and the economic potential of a patent-protected safe and effective vaccine.

With Round 1 investor funding of $3 million we can:

1. Set up our low cost-per-unit urushiol assay,

2. Determine the shelf life stability of formulation and packaging options designed to minimize costs of production,
3. Populate a cultivation greenhouse with plants with homogeneous genetically determined congener distribution patterns to build the lot-to-lot consistency required by both good practice and the FDA into our crop,
4. Validate our low cost-per-unit cultivation and manufacturing technology, and
5. Make GMP clinical trial vaccine.

We expect to need up to $10M for Round 2 to carry the company through clinical trials as descried below and in our accompanying Scientific Proposal. Round 3 funding of up to $7M will cover up-scaling manufacturing capability to produce 1,000,000+ initial treatment or booster doses per year + pay the fee for biologics license application.

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 plants in the same field from which we harvested leaves for our human proof-of-concept series vaccines, but selected to have identical or nearly identical genetically determined congener distribution. This will build he uniformity needed to satisfy regulatory requirements for lot-to-lot consistency into our crop and make compliance with the lot-=to-lot consistency requirement automatic. The vaccine 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 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

BOME Pharma Inc will be a new New Jersey C-Corporation to be formed for the purpose of commercializing this vaccine. It will form a wholly owned subsidiary, BOME Agra Inc, to take advantage of the New Jersey agricultural business sales tax exemption for the facilities, supplies and equipment needed for cultivation and drying of leaves. Dissolving the previous business entity, BOME Pharma LLC, will be simpler than converting it.

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 lower limit of 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. Source-tracing leads to a 2003 report by David Pariser et al (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 either cites nor describes a source for those numbers. 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). I tracked down Dr. Pariser’s administrative assistant to ask for information about the data source for the estimate cited in his article. She replied that 21 years after its publication Dr. Pariser can no longer remember his data source.

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. Many in this group whose severe reactions were long ago and who have successfully avoided re-exposure will want to defer allergy shots until they have another exposure. We believe that at a wholesale selling price of $300 at least 20% of this population will want the vaccine and have the insurance coverage to get it as soon as it becomes available

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 summarized his finding that 1/6 (16.7% of the population) was 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 will 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. There are adults in their 50's and 60's who report having had severe allergic reactions as children but none since that time and will not want the vaccine without recurrence. It is not possible to determine in retrospect if they were highly sensitive and lost their sensitivity over decades without re-exposures or if they were only moderately sensitive but heavily exposed from doing things kids will do. We can't attach numbers to these factors that may increase or decrease demand but we hope we have accommodated them by basing our economic projections on the most conservative of the 4 mathematical models for which we could find reasonable claims of supporting data. This is 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, 28.9M Americans, will know that they're very sensitive because of having had one or more severe reactions, and that the number of these who had a single severe reaction too long ago to want the vaccine in the absence of recurrence is at least balanced by the number of potential patients with mild to moderate sensitivity but chronic or recurrent exposure.

These 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 therefore want the vaccine. Their number may possibly equal or exceed that of the very sensitive vaccine candidates. Patients in this group will also want the vaccine more urgently than past severe reactors who are not currently having symptoms as they want relief NOW. Past one time or long ago severe reactors are like candidates for vaccines for shingles, considering a vaccine to prevent something unpleasant that may or may not 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 want the vaccine at whatever insurance leaves as their out-of-pocket cost, and begin treatment with follow-up annual boosters. We estimate 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. Those patients will not only boost total demand but also jump-start early demand. They will want protection from disease that is disrupting heir quality of life 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 utilization data @ 7/% annual growth					
	57546027	61718584	66193687	70993271	76140864
Market estimates based on minimum est 2002 utilization data @ 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 10% of mild-moderate unable to avoid = 20% addition to # severely 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 for 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. 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 $50 when the assay cost for potential competitors is `$800 will give us a functional monopoly on vaccine production until 2044.

FINANCE:

Round 1 funding for shelf life stability studies, validation of commercial scale production technology, preparation of clinical trial vaccine:

We aren't eligible for pre-clinical NIH SBIR funding because chemistry team member Prof. Yang's primary employment by a for-profit institution would make her share of project work above the SBIR limit for for-profit partner entities. We sought Round 1 funding from. venture capital companies at BioNJ's 2024 Biopartnering Conference and came home with the message that as a group they're potentially interested in our clinical trial Round 2, after we demonstrate in Round 1 that we can actually make vaccine and not just talk about it. We are therefore looking to personal contacts who know us and appreciate what we can do and to physicians who appreciate the market potential of a safe and effective allergy vaccine for PI and PO. By using available existing facilities for cultivating and processing the PI we'll need for shelf life stability studies and the manufacture of clinical trial vaccine we can reach Round 1 goals with as little as $3 million, with each $1M purchasing a 2% equity share of the company and individual shares priced at $31,250 (1/32 of $1M). We hope potential investors will find our Round 1 ratio of reasonably projected profit to risk to be attractive.

Round 2 funding for clinical trials:

Our projected funding need to carry the company through clinical trials as proposed below and discussed in greater detail in our accompanying Scientific Proposal is $7M for clinical trial costs plus an additional $2-3M for ongoing company operations including preparation, planning, permitting and tentative scheduling for the expanded facilities needed for commercial scale production. Of these we will use round 2 funds to erect an insulated 3000 sq ft cultivation greenhouse and populate it with cloned plants to be ready for commercial scale production. To the extent that we can do so without delaying their becoming operational we will defer purchase and installation of the remaining capacity expansion resources until we have clinical trial results, to let us fund them with a lower investment risk Round 3.

By Round 2 we will have met the general VC requirement of having demonstrated our ability to actually make vaccine. In addition to their stated general interest in investment at that level of accomplishment one VC company that has a clinical research organization subsidiary and invests 1/3 of clinical trial costs in companies for which it then sets up and manages the clinical trials, specifically expressed interest in investing in our company on that basis. Investment in our venture by qualified VC companies will qualify for a dollar-for-dollar match of up to $5M from the NJ Economic Development Authority's Innovation Evergreen Fund. With the FDA approval to conduct clinical trials we will have before Round 2 funds are released from escrow by our investment banker we expect our Round 2 funding to remain an attractive investment for individual and other small entity investors at a valuation of a 1% equity share in the company for every $1M invested.

We do not see satisfactory completion of pivotal Phase 2 clinical trials as a risk because the requirements the FDA already gave us for those trials will involve functionally identical subjects and vaccine and the same primary endpoint with which we achieved 90-100% efficacy with no significant adverse effects in our human proof-of-concept series (10).

Round 3 funding to expand production capacity to 1,000,000+ new patient treatment or booster doses per year:

This work, for a currently estimated maximum cost of $7M, will include pouring a concrete floor, insulating the ends and possibly providing winter gas heat for the small leased greenhouse we will have used to cultivate plants for clinical trial vaccine, as an on-site location for the drying and ethanol extraction operations which will have been performed for shelf life stability and clinical trial vaccines in the large garage behind my allergy office in Millville, 12 miles away. We will erect a modular building requiring gas, electricity, water and a septic field in which to perform on-site vacuum concentration of the ethanol extracts of dried leaves that will be our vaccine, which will have been performed in my Millville office for shelf life stability and clinical trial vaccines. Selection of storage and shipping facilities will depend on the outcome of shelf life stability studies and what we can negotiate on the basis of those studies with the

FDA. This round of funding will also include our Biologics License Application fee, estimated to be between $1 and 2M.

We will begin to solicit Round 3 funding as soon as we meet our Round 2 goal, but these funds will be held in escrow by our investment bank while we spend Round 2 funds for clinical trials and thus be at lower risk. How much lower will depend on how long we can defer drawing on them while clinical trials are in progress, to avoid delaying the commercial scale production we'll need to be able to sell vaccine as soon as we have the license to do so. If we can delay tapping Round 3 funds until clinical trial results are available, we see a Round 3 investment as attractive at a valuation of a 1% equity share of the company for every $3-4M of investment. If we will have to draw on Round w3 funds before pivotal clinical trial results are available to avoid delays in getting to market, we will tentatively value them at a 1% equity share of the company for every investment of $2M. We will know the schedule on which we have to draw on those funds and be able to set a valuation for them before we have to solicit them.

CLINICAL TRIAL ORGANIZATION & MANAGEMENT

Outreach to a sampling of Clinical Research Organizations found in a Google search for CRO's that manage clinical trials of 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 under their business model in which they invest 1/3 of the costs of those clinical trials. If that fails I should be able to put together a clinical trial network of allergists, many of whom I know personally from collaboration in the activities of the two national allergy professional societies, who already have contract clinical trial businesses affiliated with their practices.

CLINICAL TRIAL OUTLINES (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. We expect to have a more precise estimate by the time we're ready to seek Round 2 funding.

Table 2, Projected Clinical Trial Direct 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. BLA costs are included in our Round 3 budget estimate of $7M.

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 or annual booster dose if shelf life stability outcomes favor vaccine storage as an ethanol solution, up to $60 if with vacuum solvent evaporation, and sell either for a wholesale price of ~$300 at which price 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 should 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 into their stores to make other purchases will generate enough interest among the minimum estimate of 29M Americans expected 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 currently 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 to be a reasonable and conservative estimate 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 either 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, or have mild to moderate sensitivity but unavoidable chronic or recurrent exposure causing chronic or recurrent disease. 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 patients in this group with less than actuarily determined numbers of episodes or days requiring prednisone per year and refuse to give them vaccine costing $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%.

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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.

None of the above calculations include mildly or moderately sensitive patients with chronic or recurrent exposure because we do not know how numerous these patients are. We can conclude that they are numerous however, 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 cost of vaccine at any of the above price points.

INVESTOR OPPORTUNITY TO PARTICIPATE IN OUR NEXT FDA PRE-IND MEETING

While a small business entity wanting to develop an FDA-regulated product normally gets one free pre-IND meeting, the FDA already offered to give us a second. We will use this meeting to request review of our initial proposals for vaccine lot content and tolerance specifications (based on what we'll have produced and decided to bring to clinical trials) and for requirements and specifications for clinical trials. The process consists of an applicant submitting a detailed written list of questions he or she wants the FDA to address, a 2-3 month lead time for scheduling, and then what was formerly a conference call but will now be a Zoom meeting at which we and the FDA's multi-specialty team will discuss rhe questions we submitted. They then prepare a ormal written response, which we receive about a month later.

We will welcome questions or concerns from any investors or potential investors who have them, to incorporate into our list of questions to submit. We can't ask the FDA to our talk with individual investors during the meeting but we can either include the substance of every investor question in our requested meeting agenda or tell you and offer to discuss with you any reasons we may have not to want to accommodate your request. Any interested investor or potential investor will have the pportunity to watch he meeting in view only mute mode.

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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