

A Proposal for
Orphan Pharmaceuticals Inc.
A Psychedelic Medicine Pharmaceutical Corporation

Prepared by
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July 27, 1985
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"MDMA is an orphan with nobody bidding to be its parent."

Dr. Jack Downing, Time, June 10, 1985, Page 64.

"Until now."

Rick Doblin, July 27, 1985.

"For a variety of reasons, these drugs (agonists and antagonists) and others that are used to treat chronic drug addiction have not been attractive development prospects for the private sector. Thus, they are referred to as "orphan" drugs. The Strategy continues to encourage the pharmaceutical manufacturers, colleges and universities, and professional health care organizations to sponsor more research on orphan drugs. The Food and Drug Administration now has an Office of Orphan Products Development which is assisting in this area."

1984 National Strategy for Prevention of Drug Abuse and Drug Trafficking
White House Drug Abuse Policy Office

"Inexperience has also created the position where, now that publicity is being given to our journey which once roused thousand to ecstasy, it is not only forgotten but a real taboo is imposed upon its recollection. History is rich in examples of a similar kind. The whole of world history often seems to me nothing more than a picture book which portrays humanity's most powerful and senseless desire - the desire to forget.

The Journey to the East, Hermann Hesse. 1932.

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A report on the creation of a psychedelic medicine pharmaceutical company

Rick Doblin

My two main areas of interest are in facilitating MDMA research right now, and in exploring the possibilities of creating a legal pharmaceutical company. As far as the research goes right now, Earth Metabolic Design Foundation is initiating the animal studies required by the FDA prior to human testing. There will be two four week chronic toxicity studies, in both the dog and the rat, costing about \$60,000. Preliminary studies in rats suggest a wide margin of safety and a very significant therapeutic index. Though the preliminary studies failed to find any evidence for brain damage, there will be a special emphasis on further investigating this possibility.

These studies will help in several ways, and thus are the best step forward at this time. The move into FDA required studies is a move into the system, and will strengthen the opportunities of the doctors to do research. The two studies will demonstrate our serious intent to seek the rescheduling of MDMA. The sooner we can move into human research the better, and physicians at major universities are considering undertaking some of the initial research. Also, any further confirmation of the safety of MDMA when administered under medical supervision will help greatly in the DEA hearings and the public mind.

The second project is the creation of the pharmaceutical company.

It is my impression that if a prospectus were created in accordance with SEC rules an underwriter might just possibly raise \$10 million for MDMA-related research. The first step is the creation of a prospectus, which would cost about \$350,000 to prepare. About \$150,000 of that could be raised from gifts donated non-profit to fund research directly. The interlocking of profit and non-profit here makes it all the more likely to work well, research gets paid for through non-profit tax deductible foundations, and the research is in the public domain, aiding anyone who wants to build upon that work. Since a fundamental goal of this work is responsible medical use of psychedelic medicines, additional "competition" is welcome. Any profit making vehicle can step in at any point, researching in any direction and keeping the next levels of research proprietary.

The outline of expenditures is as follows- \$60,000 FDA-required studies in the rat and the dog, \$50,000 for human Phase 1 and 2 studies hopefully in Cambridge and in Sarasota, \$40,000 to fund a WHO-cosponsored international conference on psychedelic research. These are goals and distinct possibilities. The initial animal and human studies will take about a year, and the prospectus could best be sold after initial reports indicating efficacy and safety under medical supervision were in hand.

Also, \$200,000 for legal fees, accountants and the writing and research of all the issues involved in creating the prospectus to SEC standards. Research includes designing and pricing out the complete series of tests that might need to be completed prior to FDA approval.

The non-patentable status of MDMA deserves some analysis. Though MDMA could not be patented, a version of MDMA designed for maximum assimilation into the body could be. Any company wanting to market simple MDMA would have to take their formulation

through animal studies costing about \$2.5 million, which is not too large to stop any company but would still slow them down more than a year. In February, a New York physician received a specific use patent for ibogaine, in the treatment of heroin addiction. This means that it might be possible to receive use patents for MDMA. Just as important is the precedent created of the use of a psychedelic in the treatment of drug abuse, one of the most promising areas of MDMA therapy which has not gotten a lot of credence yet from NIDA or DEA or FDA officials. Also, THC is being marketed now by Unimed, a publically traded company, though THC is not patentable. However, the specific method used in its synthesis is patented. Initial market penetration gives an advantage to the first company.

Also, there are several new compounds that could be patented that deserve experimentation. The first research project of the newly formed company would be to explore various possible chemical modifications of the basic MDMA molecule, and to seek to determine which substance to put through the lengthy testing process. It would be desirable if the compound chosen could be patented, but if MDMA proves to be the most useful in psychotherapy it will be the compound that gets worked with first.

Though the reports on a new compound being tested are mixed, several people felt that the new compound might be almost as therapeutic as MDMA and less abusable. It has less of an effect on the heartbeat and blood pressure, and is a bit more subtle with a little less of the warmth of MDMA, thus being less likely to be significantly popular but still insightful and positive and certain to be very helpful in psychotherapy. The first company to begin work in this area would have the support of the chemists and would be able to research all the new compounds, and thus a large company could be built up over time with several substances on the market at the same time. The potential here is large, but there is a risk and how the social winds blow will play a large part in the success or failure of this venture capital project. But, it seems to me to be likely to succeed in time, and worth the investment of time and money.

The eventual distribution of MDMA would likely be to approved physicians and psychotherapists working within licensed inpatient facilities, modeled on hospice centers and methadone clinics. From a financial point of view, there is more profit to be made in the centers than with the pharmaceutical company, since the MDMA may eventually cost \$5-10 per dose while the therapists charges may amount to several hundreds of dollars. Therefore, a division of the pharmaceutical company will be devoted to owning, building, staffing and managing some of these centers of treatment.

Since I have the time, and the contacts to coordinate this, I have asking myself if I have the desire. I am not certain, but I think that I do. My political goals of aiding psychiatry and the culture to integrate emotions and reason are well served by working on the pharmaceutical company. It is one of the few possible ways to raise research funds, since neither the government nor the pharmaceutical industry is likely to fund studies at this time. Also, the interlocking non-profit foundation provides a means whereby the \$10 million cost of research could be partially funded by donations from private foundations and individuals, making the development costs less and the potential return on investment greater, although there would be more competition, which would be great.

Of course, not all of the \$10 million needs to be raised publically. The more the initial investors put in, the greater percentage of the stock they can own. If investors wanted to, they could invest the first \$1-2 million in research, have the company created so that it could either go public or remain private depending on a financial evaluation done after more of the research was in and with additional information about the direction of our changing cultural attitudes over the next year or so. If the initial research in human subjects was fruitful and was with cancer patients and those in pain or terminal for any reason, the marketability of MDMA would be almost certain.

At this point, \$150,000 of the \$350,000 initial seed money is pledged. Five or six more investors are sought to contribute the remaining expertise and \$200,000.

Any comments that you care to give concerning this project would be meet with great curiosity.

Rick Doblin 2105 Robinson Avenue, Sarasota, Florida 33582

Funding for MDMA Research

- 1. Total Research costs to evaluate MDMA to the satisfaction of the FDA so that MDMA can be a prescription medicine are estimated to be \$10 million, with significant variations possible.**
- 2. A pharmaceutical company can be created to investigate MDMA and other psychedelic medicines. A stock offering could be developed for about \$350,000 and would perhaps result in the successful acquisition of the venture capital.**
- 3. Animal studies are currently underway, and initial results suggest no brain damage in rats from a single oral administration of 400 mg/kg of MDMA, nor from chronic administration either. Studies evaluating self-administration of MDMA in monkeys are underway and they will have a bearing on the perceived abuse potential.**
- 4. A four week MDMA chronic toxicity study in rats will be completed**

about October and cost about \$30,000.

5. An additional \$30,000 will need to be spent on studies in dogs before human work can begin. This study is also seen to be underway.
6. Prior to human studies, methodological issues of psychedelically-assisted psychotherapy research will have to be addressed and at least partially resolved. A World Health Organization and Earth Metabolic Design co-sponsored conference is a potential, and would cost about \$40,000 to fund.
7. Phase one human studies might be done in Sarasota, and will cost about \$20,000. These studies will take about three months from initiation.
8. Phase Two human studies may possibly be done in Sarasota and Cambridge. They will cost about \$30,000. These studies will also take about three months from initiation. Target date for completion May 1986.

- 9. After the Phase 2 human studies, future research should be funded from the public offering. Public offering to be ready hopefully by June of 1986.**

- 10. Total required for legal, accounting and research to bring the Psychedelic Orphan Drug pharmaceutical company to the point of a public offering is \$200,000, with funds already discussed making a total of \$350,000. Also, some gifts of funds towards these ends can be donated to a non-profit foundation and are tax-deductible, making the possibility that MDMA will become a medicine more likely by providing more ways for people to contribute.**

- 11. Depending on how the social winds blow, return on investment could be very significant in the long term.**

- 12. If the venture capital offering succeeds or not, the information gained from the first \$350,000 phase will have lasting scientific implications.**

Proposed Stock Distribution for Orphan Pharmaceuticals Inc. Phase 1

500 Series A shares will be issued at a par value of \$1000.00 per share.

300 Series A shares will be sold to Phase 1 participants for \$1000 per share.
200 Series A shares will be awarded to the two foundations listed below

Both the as yet unnamed Foundation emerging out of the Arupa group and the Multidisciplinary Association for Psychedelic Studies (MAPS Foundation) emerging out of Earth Metabolic Design will be issued 100 shares each. The stock will be held in trust by Earth Metabolic Design until those foundations are legally functioning.

Funds will be spent as they are raised.

When the prospectus has been created, Phase 1 will be concluded.

Proposed Stock Offering for Orphan Pharmaceutical, Inc.

Phase 2

The as yet undetermined underwriter may make some suggestions towards changing this proposal. A Phase 1 stockholders vote would be held to determine the ultimate form of this offering.

1,500,000 shares of Series B will be issued at a par value of \$10 per share

1,000,000 shares of Series B will be sold through underwriting at \$10 per share
500,000 shares of Series B will be awarded to holders of Series A, at 1000 to 1

When the prospectus is fully subscribed for \$10 million, Phase 2 can begin. If the present spirit of cooperation between the government and the researchers continues, Phase 2 may end in five years with MDMA becoming an FDA-approved medicine that is placed in Schedule 3, and marketed by Orphan Pharmaceuticals.

Filling a related marketplace demand, Valium was put on the market in 1963. The patent protection didn't expire until this February, permitting Valium to earn over three billion dollars for the Hoffman-LaRoche Pharmaceutical Company.

Psychedelic medicines will not be prescribed to such a degree, due to their very intermitent therapeutic use pattern compared to an often daily dosage of Valium. However, there is a significant market if research and treatment can meet social standards.

Kansas City—A Quiet Confrontation DEA Hearings—July 10-11, 1985

Between the initial clash in Los Angeles and the final flourish of experts in Washington, the city of power, the Drug Enforcement Administration hearings in Kansas City on July 10 and 11 were a model of polite, cooperative legal proceedings. Nothing much was changed, nothing very dramatic happened, and the balance of power was sustained. Just like in historical Kansas City itself, the pioneers paused to rest and the hearings were conservative and competent. I even fell asleep at one point, an alternate state of consciousness approached by many during a prolonged and rather redundant cross examination. There were, however, highlights and in the quiet give and take a few rather significant trends emerged, made all the more remarkable because of the ease and lack of controversy with which they happened.

Primarily, there was movement in the direction of an agreement that MDMA had a therapeutic index which would indicate that some human studies are justified. The studies of Dr. Seiden of the University of Chicago still suggest some causal relationship between MDMA and nerve terminal death, although there has never been any evidence at all of any functional consequences of the observed effects. The U. of C. results need to be viewed with a certain tentativeness about what actually is suggested since they were not replicated by the Intox Laboratories study which failed to show any nerve tissue damage in rats orally given an escalating amount of MDMA for 12 days, beginning with 25 mg./kg. the first day and ending with 300 mg./kg. on the last. The Intox Lab study orally administered MDMA to the rats for 12 days, in contrast to the U. of C. study which injected much lower doses for a much shorter time period. Since the INTOX study should presumably reveal more damage than the U. of C. study, the lack of any observable damage suggests a greater degree of safety than one would expect from the warning of the DEA of possible permanent brain damage from one average size 100 mg. amount of MDMA. Also, the INTOX study has established the LD 50 orally as 325 mg./ kg. When all studies are looked at together, the doses that may cause damage in humans are in excess of the anticipated therapeutic dose by a factor of, at the most conservative, about ten. On the witness stand, Dr. Seiden stated that there was no scientific justification for prohibiting research to proceed in humans.

There is an awareness on the part of the DEA that FDA required chronic toxicity animals studies are underway, and that permission for human studies will be requested. There is an awareness on the part of the physicians and researchers that if the protocols for the human studies are sufficiently rigorous, permission will be forthcoming. Upon reflection, I feel and know that during the course of this hearing the idea of human studies moved through the resistance and became conceivable by all concerned. As a result of this debate, human studies moved into possibility as quietly as a sailboat entering a harbor on a clear, calm moonless night.

Of greater potential significance, and with even less fanfare, were discussions outside of the cross-examination process concerning the development of our own

pharmaceutical company. This idea met with cautious approval by Frank Sapienza from the DEA administrators office, and Steven Stone, the DEA lead attorney. I gave Frank Sapienza a five page discussion of the strategy and steps I plan to take in building the company and he will review it for possible comments and critiques. I told Steven Stone, for his information, that the origins of the FDA requirements went back to the Nurenborg Trials and Conventions formulated after WWII in response to the Nazi human "medical" experiments. I demonstrated to Steven Stone my respect for the FDA guidelines, and I think he supports controlled human experimentation, and thought the idea of forming a pharmaceutical company valid.

The testimony of Dr. Rick Strassman bore on the fate of this company directly, for he works in a research project with cancer patients who are administered THC for their nausea from chemotherapy. He told about the superior quality of smoked marijuana over a THC pill for relief of nausea, and the political controversy that made the smoked form of this medicine unavailable. He spoke about the scientifically unnecessary 15-20 year development process, and even Steven Stone recognized that the political controversy surrounding marijuana has obstructed medical research. Trying to show that the government did not obstruct Schedule 1 researchers, Steven Stones' questions to Dr. Strassman backfired as it was revealed that Dr. Strassman has been waiting for his Schedule 1 approval for many months, and wonders what is causing the delay. These points were not lost on Judge Young.

Though major challenges (problems) are certainly ahead, forming a pharmaceutical company clearly is the vehicle for forward movement. This concept was tested at the hearings, and survived intact. Richard Cotton said he is interested in acting as council, Tom Roberts is ready to work full time on all aspects of preparing the prospectus, and others are supportive. An idea whose time has come quietly (for now), the psychedelic medicine pharmaceutical company passed through the seive of the DEA filter, and is now more viable than ever.

Richard Cotton, our lawyer, Debby Harlow and Tom Roberts of EMD, and the witnesses Dr. George Greer, Dr. Dave Nichols, Dr. Rick Strassman, and June Reidlinger, R.Ph. were in Kansas City the day before the hearings, reviewing testimony, role playing and sharing new information. It was here that it became clearer to me how I had caused others to feel threatened by my talking to the press about my experience. I sense correctly (in my mind) the importance of challenging the DEA definitions of drug abuse, but lack the eloquence and credentials to get my views across. By stating a case that some of the witnesses actually believe but feel impolitic to state, I leave them open for crossexamination and possible criticism.

As each witness thought about the inevitable question from the DEA about their own use of MDMA, they found that conditions under which a favorable decision is made concerning the appropriateness of taking MDMA varied. However, the only conditions deemed appropriate at all by the DEA are when MDMA is used by a doctor to treat an illness. A strategic, expedient decision designed to enhance the credibility and

authority of the witnesses was made. They would formally call legitimate only the use of MDMA under medical supervision. The DEA's definition of recreational use as all non-medical was conceded to. This was then railroaded by the DEA logic train into the conclusion that therefore non-medical use was abuse. The witnesses thus supported the scheduling and criminalization of MDMA. When Steven Stone started asking questions concerning the potential of MDMA as aids to creativity or religious inspiration, the witnesses testimony judged these uses of MDMA inappropriate. There was even agreement that there would probably be significant adverse public health consequences.

The point of view that there are positive public health consequences that far outway the cases of genuine abuse or harm was left unstated, and tacitly denied. The additional point of view that drug laws and scheduling are in themselves severely toxic to the public health was not officially raised even in passing. This issue is, as Phil Donahue would say, " a whole other show", but of such primary importance that I cannot leave it unaddressed .

There were many especially enlightening comments, but my favorite was from Judge Young. After the testimony of Dr. George Greer, Richard Cotton asked if arrangements could be made so that Dr. Dave Nichols could testify next. Steven Stone said that on his schedule Dave Nichols was next anyway. Looking at Steven Stone, Judge Young laughed and replied, " Its not the first time I'm the last to know" The reference was to the Emergency Scheduling Action which took effect July 1, which temporarily preempted the hearings process as far as deciding on the proper scheduling of MDMA.

All in all, Kansas City was evenly supportive of both positions. Of significance is the local Kansas City TV News report on the hearings, which was strongly supportive of the concept of research, and which discussed both the animal studies of Dr. Seiden and associates and that of Intox Labs. A way has been cleared, a window of opportunity has been opened, and it is up to those that care to find the means to move forward.

Enclosed is a revised copy of the proposal that you saw at Jack Downings' home in San Francisco. I would greatly appreciate your comments. You mentioned the possibility of a meeting the weekend of September 7-8, and though I am not sure of my responsibilities at school yet, I think that I might be able to visit during that time if developments warrant such a meeting.

I've written to Earl Belle concerning his interest in participating in the development of MDMA as a medicine, as well as in the general development of other compounds for the field of psychedelic medicine. I am sure that he appreciates the speculative nature of the business aspects of this project, and I hope that he also appreciates the scientific, therapeutic and spiritual aspects as well.

I have just come into the possession of an offering seeking \$250,000 for the development of a generic pharmaceutical. That offering is about 90 pages, and is in appropriate legal form. The Orphan Pharmaceuticals proposal is one generation removed from such sophistication, but must move in that direction. However, the basic concept can be seen in the proposal that I am sending you.

I look forward to hearing from you and hope that we can meet to help further this important work.

Psychedelically yours,
Rick Doblin *Rick*

2105 Robinson Avenue
Sarasota, Florida 33582

Dear Editor,

July 1, 1985

Your June 24th issue discussed MDMA, a chemotherapeutic adjunct to psychotherapy. Also mentioned was Unimed, a publically traded company that markets THC for the treatment of nausea in chemotherapy. As MDMA becomes a Schedule 1 drug, the only appropriate response by those interested in its use is to do the FDA research to justify its use as a medicine. Therefore, a venture capital stock offering is being planned to raise the \$10,000,000 for research required prior to an FDA decision regarding its rescheduling.

The company, tentitively named Orphan Pharmaceuticals, will raise funds for research for both patentable and unpatentable compounds for use as adjuncts to psychotherapy. It is my hope that the business community will critique and advise in the development of the company so that it can become more than a dream.

Also, there was a major misstatement of fact concerning the research cited by the DEA to suggest that MDMA causes brain damage. The U. of Chicago study injected MDA, not MDMA as the article stated, in rats. Several drugs currently approved by the FDA for daily use in children cause similar brain damage when injected in rats, and the medical community has decided that the rat brain and the human brain act significantly different to make the rat studies largely irrelevant. Also, a recently completed study by Intox Labs, Redfield Arkansas, administering MDMA orally to rats demonstrated that even a human equivalent dose of 25 grams caused no brain damage in rats.

Sincerely, Rick Doblin