Breakthrough Therapy Designation: Streamlining the Path to Approval

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What springs to mind when you hear the word "breakthrough"? The light bulb? The printing Press? The telephone? Nuclear fission? What about fire? What about consciousness itself? That's more like it. When did we wake up? In all likelihood, immediately following our becoming conscious[1] was our awareness of trauma, danger, pain, and suffering. Whether it's the trauma of being born and entering the world, watching those around us leave the world through disease or other hardship, hordes of pillaging marauders, horse archers, tiger attacks, or the existential threat of life itself, life is suffering. For as long as we have been conscious beings, we have had to deal with trauma—both physically and mentally.

Therefore, discovering a method paired with a molecule—MDMA-assisted psychotherapy—that can heal trauma of the mind—post-traumatic stress disorder (PTSD)—is by nature healing suffering, easing suffering, changing the human condition. That is not only a breakthrough, but a miracle[2] of science, nature, and multidisciplinary collaboration.

Quoting Richard Carter's history of the discovery of the polio virus, Steven Pinker points out that on the day it was announced "people observed moments of silence, rang bells, honked horns, blew factory whistles, fired salutes, …took the rest of the day off, closed their schools or convoked fervid assemblies therein, drank toasts, hugged children, attended church, smiled at strangers, and forgave enemies." (Pinker, 2018, pp. 64–65) Perhaps it's time to understand the level on which this new breakthrough will change the human experience. In addition to healing individuals with PTSD, the ripple effect of mending this type of trauma on families, acquaintances, and even strangers, is going to be exponential and likely immeasurable. Maybe it is worth considering a day off to celebrate as a species. No gifts or cards, just a celebration of science and achievement in improving the human condition.

Many breakthroughs come in the form of multidisciplinary endeavor. No wonder that the first time in human history that a psychedelic compound has been run through a scientifically rigorous clinical trial process, it's been with a multidisciplinary approach, combined with the unstoppable will of one man (Rick Doblin), combined with the compelling mission, and so many other reasons.

In August of last year, the Multidisciplinary Association for Psychedelic Studies (MAPS) was granted Breakthrough Therapy Designation by the U.S. Food and Drug Administration (FDA) for the treatment of PTSD with MDMA-assisted psychotherapy. That in and of itself is a breakthrough: a breakthrough for thorough, well-communicated, and transparent scientific rigor. That a small non-profit organization was able to make that happen is even more astounding.

Here's what I know for sure, based on my experience. It is really $@&! hard to get a drug approved. Years of rigorous science. Years of rigorous analysis. Years of

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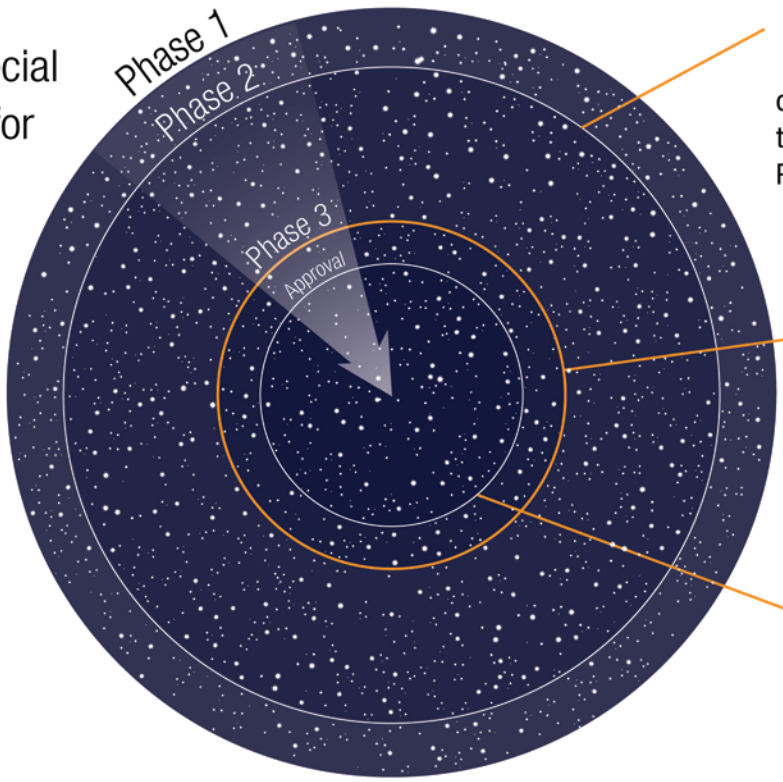
[1] Depending on your religious background and many other factors that try to figure out consciousness

[2] Miracle in this instance is a somewhat loaded term. For my purposes, I mean something we don't yet understand, not that there was necessarily divine intervention involved…though, I can't completely dismiss that notion given the possibilities that exist in the universe…truth is, I really don't know…and neither do you…isn't that fun?

The Universe of FDA Drug Approval

On July 28, 2017, MAPS and the FDA reached agreement on the Special Protocol Assessment for Phase 3 clinical trials.

The chart depicts all studies that have entered the FDA drug approval process as represented by stars. Studies are placed according to how much of the approval process they completed. This means that all stars in the outer layer represent studies that did not advance after the Phase 1 trials. Stars in the inner layer represent drugs that have been approved by the FDA for the market.



78%
of all the drugs make it through Phase 1 to Phase 2

20%
of all the drugs are accepted for Phase 3

12%
of all the drugs are approved for the market

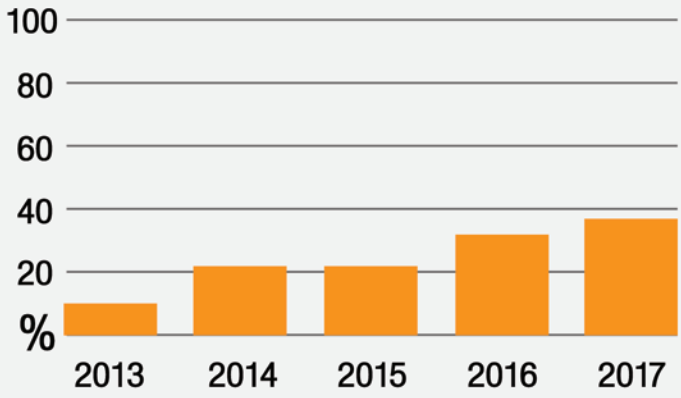
Source: Wong CH, Shaw K., Lo A. (2018) Estimation of clinical trial success rates and related parameters. Biostatistics (prepublished). Numbers from 2000 to 2015, with oncology excluded.

BREAKTHROUGH THERAPY DESIGNATION (BTD)

On August 16, 2017, the FDA granted Breakthrough Therapy Designation to MDMA-assisted psychotherapy for PTSD.

approximately 30% of the requests for BTD are granted by the FDA

The BTD program was launched in 2012. The chart below shows the percentage of novel drugs designated as Breakthrough Therapies for each year.



Source: FDA.gov novel drugs summaries for the years 2013-2017

rigorous planning and brainpower. To watch MAPS work towards its mission is to witness the coming together of the right minds, the right ideas, the right conversations, and the right circumstances over and over and over again, every step of the way. MAPS is all about synchronicity and willpower. From the organization's humble beginnings and mission of human wellness, it has achieved the legitimacy that comes with this type of recognition from a federal health authority.

By pursuing the scientific, federally regulated route to legitimizing psychedelic therapy, MAPS is using the rules of the system to break new ground. This required following the rules and also knowing what questions to ask along the way. MAPS challenges authority with a thoughtful and fact-based approach, instead of just rebellion for rebellion's sake. This attitude has enabled MAPS to get answers to questions that have not been asked before, since nobody else has brought this substance through the process. Any number of hurdles were overcome due to the right effort by the right people, many of whom genuinely have had a personal interest in the outcome because of their own experiences with trauma, mental illness, or psychedelics.

Is there something to be said for a personal breakthrough that comes through the psychedelic experience having an impact on understanding fundamentally, what a drug does? This is another part of the breakthrough of MDMA-assisted psychotherapy—that many of the therapists in the Phase 3 trials have actually had the chance to experience the treatment themselves, in MAPS' ongoing Therapist Training Protocol. How many of the scientists that are studying current psychiatric medicines and their effects on the human psyche know what it's like to use these treatments themselves?

When I asked a good friend and former colleague, Julie Lepin (currently Senior Vice President of Regulatory Affairs at Celgene Corporation) about Breakthrough Therapy Designation (BTD), her response spoke volumes: "It's a pretty big deal," she said. "BTD reflects the FDA's assessment that the early data provided are outstanding (knock-your-socks-off as I heard one reviewer describe the need) and likely reflect a significant therapeutic advance. In having BTD they commit to working closely with the sponsor to progress the new therapy because of this perceived advancement, so that patients in need can get early access to it."

There is an exciting and daunting future ahead for the MAPS Public Benefit Corporation (see my previous article in MAPS' Spring 2016 *Bulletin* for more about how the benefit corporation works). There is a tremendous responsibility to carry out the mission of the organization with ethics, integrity, transparency, and social good for all mankind. MPBC has the heart of a non-profit, with the structure of a for-profit business anchored to a social benefit mission to change the way humans heal from trauma.

MAPS and the MAPS Public Benefit Corporation had already attained legitimacy through the diligence and perseverance of the team at MAPS, as well as the undeniable efficacy of the treatment we have seen so far in Phase 2 trials. But progress through protocol reviews and favorable results in small studies are typical in early stages of drug development, and sometimes even through the later stages for products moving through the regulatory lifecycle. By highlighting a treatment through BTD, and distinguishing it among other treatments, is something very special. As a founding Board member of MPBC and advocate of the work that MAPS has done since 1986 to bring us to this point, I could not be prouder to be associated with this progress. PTSD and mental illness have touched my family in a real way, and I am proud to imagine a day in the not-so-distant future where this treatment will be readily available for those in need.

Where will MAPS be in 50 years? In one of my favorite books about long term thinking, The Clock of the Long Now (Brand, 2000), Stewart Brand outlines how a thought experiment spawned innovation. The idea is of humankind facing the complex, yet simply stated question: "How do we build a clock that would last 10,000 years?" Well, where would we put it? How would we tell others who came after us how to maintain it? Where do we get replacement parts? This barely scratches the surface of some of the questions Brand explores. The yield is technology, innovation, and breakthroughs of all kinds simply because that is what humans do:

We try to solve problems. As Steven Pinker points out in Enlightenment Now, "progress is an outcome not of magic but of problem solving."

MAPS is trying to solve a big problem: the problem of healing trauma. We now have institutional proof that what many have thought for a long time could be a breakthrough of infinite importance, can be officially filed (with paperwork and everything) as a Breakthrough with a capital B. And that is a big deal.[3]

Matthew J. Neal *currently works as the Sr. Director of Product Management in Regulatory Solutions at PAREXEL and serves on MPBC's Board of Directors. He previously spent more than a decade at Amgen, Inc. as Director of Operations in Global Regulatory Affairs & Safety with a focus on Human Therapeutics to dramatically improve people's lives. Prior to that, he lived in Philadelphia where he was one of the pioneering members of the Regulatory Submissions Department for GlaxoSmithKline. Matthew has been publishing and submitting electronic dossiers to the FDA since 1996, and submitted the very first fully electronic NDA for GSK in 1999. Matthew holds a Master's Degree in Communication from Temple University. He can be reached at matt@mapsbcorp.com.*

[3] In conjunction with the Breakthrough Therapy Designation, MAPS also received a Special Protocol Assessment – which, in some ways, is more of a big deal than Breakthrough Therapy—doesn't sound as sexy, but it's a big deal. It basically means that based on the protocol design, assuming that we have the anticipated outcomes that were illustrated in the Phase 2 trials, just on a larger scale and without any new significant safety concerns, that we have an approvable product in MDMA-assisted psychotherapy. (https://en.wikipedia.org/wiki/FDA_Special_Protocol_Assessment)