

## Phase II/III, Randomized, Double-Blind, Placebo-Controlled Trial of Snapeacillium for Quidmort

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**Sponsor: Gryffindor Pty, Ltd**

**Background:** Government scientists have known for a long time that about one in 1000 individuals has unique mental abilities such as telekinesis, divination, and metamorphosis. For centuries these abilities were attributed to magical influences. In 1998 H. Potter and co-workers identified genetic variations of the MuGL (pronounced “muggle”) gene as the etiology of these abilities. Soon after identification of the gene, a new disease called Quidmort was described that was found to cause loss of special abilities. Quidmort causes prolonged sneezing and hiccups, but no significant clinical morbidity. There are no FDA approved medications which are effective in treating Quidmort. While there is anecdotal evidence that ingestion of large quantities of chocolate frogs causes mild and transient return of some magical abilities in infected individuals, this has never been studied formally. Nonetheless, most patients with Quidmort use this remedy. Infected individuals face a loss of livelihood and ostracism; most are forced to leave their community and relocate.

Recently an unusual virus, QM-1, was identified as the cause of Quidmort. Scientific debate continues over whether the QM-1 virus is natural or artificial. The mechanism by which QM-1 interferes with magical abilities is also unclear, but it seems to inactivate the MuGL gene, thereby decreasing or abolishing special abilities. Whether the effect of QM-1 on the MuGL gene is reversible is not known.

Snapeacillium, a member of the class of antivirals known as necrolides, has been developed to treat patients who have lost their special powers due to Quidmort. Snapeacillium blocks the activity of the QM-1 virus in infected individuals, through process known as “Dumbledoreing”. It is speculated that blocking QM-1 will in turn allow expression of the MuGL gene and result in partial or full return of special powers. Snapeacillium is the first agent to be tested in humans for treatment of Quidmort.

**Pre-clinical Data:** The components of Snapeacillium are proprietary, but consist at least of blast-ended newts, beetle powder, and ampicillin.

Teratogenicity studies in animals have not been performed, but similar newt-based products have not been associated with fetal defects (though there has been a tendency for pups born to mother rats receiving eye of newt to lose their tail after birth).

Snapeacillium was the subject of extensive pre-clinical tests in bats, the only animal model that exhibits symptoms with Quidmort virus infection. (The test studies were performed in accordance with IACUC procedures.) The LD50 was 50 mg/kg, approximately 25 times greater than the proposed dose of 2 mg/kg. At this dose, no adverse effects were observed, except a 15 percent increase in the rate of biting animal handlers (not statistically significant) and a tendency of some bats to fly backwards. Based on a comprehensive pharmacological analysis, neither of these side effects is expected in the human subjects. Post-mortem studies showed that Snapeacillium-treated bats had a 97 percent reduction in QM-1 viral load and significant reduction in Quidmort symptoms. Effect on magical abilities in the bats was not assessed.

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**Clinical Data:** Snapeacillium was administered to eight subjects in a phase one trial. These subjects were given Snapeacillium, and then monitored continuously for an eight-day period. The drug was generally well tolerated. There was a moderate increase in liver enzymes (to 3x upper limit of normal) in 40% of subjects, and a marked increase (10x ULN) in one subject. The enzyme levels returned to slightly above baseline after one month, and no adverse physiological effects were detected. It was noted that one subject became partially hypnotized when observing lumen, but the effect was transient.

**Study overview:** This study is a randomized, double-blind, placebo-controlled trial of a new treatment agent. A total of 60 adult subjects will be enrolled into the clinical trial; 30 subjects will receive the therapeutic agent and 30 will receive placebo. The QM-1 viral assay will be performed at the Hogsmeade Clinical Laboratory, a CLIA certified site that meets the standards of OMN, the pre-eminent professional society for esoteric laboratory testing, and has been validated in accordance with laboratory procedures. However, the test is not FDA-approved. The data from this study will not be used towards receiving FDA approval for the QM-1 viral assay by the Hogsmeade Clinical Laboratory.

Because the effect of Snapeacillium on a fetus is not known, all women of child-bearing potential must use two forms of contraception, one of which must be hormonal based.

Subjects who meet the inclusion and exclusion criteria will be invited to participate. Those who provide informed consent will be randomly assigned to receive a single dose of either 2 mg/kg of Snapeacillium or placebo. The randomization scheme will be 1:1. Gryffindor Pty, Ltd will complete the randomization assignment and provide each site with an equal number of doses of both Snapeacillium and the inert placebo tablet. Each dose will be labeled with a sequential number, starting at number 001. The doses will be dispensed in the same sequential order as subjects are enrolled in the study (i.e. the first subject to be dosed at a site will receive the dose numbered 001, the second subject to be dosed will receive the dose numbered 002 and so on). Subjects assigned to either arm must not utilize any other therapy for Quidmort (including chocolate frogs). Subjects will be monitored every month for six months with routine physical exams, blood and urine tests (analysis also performed at the Hogsmeade Clinical Laboratory), measurement of QM-1 viral load, and the Magical Ability Score (MAS), which measures special abilities. The Quality of Wizard Life (QOWL) survey will be administered at enrollment and last visit. Subjects withdrawing from the study prior to final scheduled visit must return to clinic for exam, MAS, and QOWL. In addition, their clinical course will continue to be followed for 1 year by medical record review.

Because the QOWL is only available in English, patients who do not speak English are not eligible to participate.

Subjects will be paid a total of 100 galleons (1 galleon = 6.64 USD) for participating. They will receive 10 galleons for each of the first six visits and 40 galleons at the last visit.

The sponsor of the study, Gryffindor Pty, Ltd. will study Snapeacillium at one domestic site (Salem, MA) and one international site (Hogwarts, UK). Both of these locations have a high incidence of Quidmort. There will be a total of 60 subjects randomized. The principal investigator is Dr. J.R.R. Rowling, who has received a Ph.D. in pharmacology from Oxford. Dr. Rowling helped develop Snapeacillium, and has a patent pending for this drug. All study personnel have received GCP training from the IRB staff.

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Schedule of events:

| <b>Event</b>                         | <b>Visit 1</b> | <b>Study visits 2-5</b> | <b>Study Visit 6</b> | <b>Early Withdrawl Visit</b> |
|--------------------------------------|----------------|-------------------------|----------------------|------------------------------|
| Informed Consent                     | X              |                         |                      |                              |
| QM-1 viral assay                     | x              | x                       | x                    |                              |
| Pregnancy Test <sub>a</sub>          | x              | x                       | x                    |                              |
| Physical Exam                        |                | x                       | x                    | x                            |
| Blood Draw                           |                | x                       | x                    |                              |
| Urine Collection                     |                | x                       | x                    |                              |
| Magical Ability Score(MAS)           |                | x                       | x                    | x                            |
| Quality of Wizard Life Survey (QOWL) |                | x                       | x                    | x                            |
| The Boggart Banishing Spell (BBS)    | x              | x                       | x                    | x                            |
| Randomizaion                         | x              |                         |                      |                              |
| Study Drug Distribution              | x              | x                       |                      |                              |
| Study Drug Collection                |                | x                       | x                    | x                            |

- a. Serum pregnancy test will be done at screening and a urine pregnancy test will be done at all follow up visits.

**Inclusion Criteria:**

- Documented prior magical abilities through the Ministry of Magic Witch and Wizard Registry
- Detectable QM-1 virus in blood.
- >= 18 years
- </=120 years
- Able to sign informed consent
- Willing to attend all visit

**Exclusion Criteria:**

- Detectable Harry Potter virus in blood
- Suspension of powers through the Ministry of Magic Which and Wizard Registry
- Unable to consent in English

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**Recruitment:** Subjects will be recruited through advertisements in various publications, such as *The Daily Profit*. The advertisement will simply state: “Volunteers needed for clinical study to determine the effectiveness of Snapeacillium, an exciting new therapy for Quidmort. For more information about this important clinical study call 1-800-THERAPY.”

Additionally, information will be requested from the Ministry of Magic Witch and Wizard Registry if enrollment efforts are not successful through advertisements alone. The Ministry of Magic Witch and Wizard Registry is controlled by the Ministry of Magic, Salem MA. Individuals request to be entered into this registry when they realize their magical powers. Entry into the registry is contingent on the applicant successfully completing a series of assessment and tests that are administered by the Ministry of Magic. The registry was developed to promote networking, provide a platform to quickly disseminate educational and informational materials and connect witches and wizards from around the globe. Approved members of the registry have access to all of the information contained within the registry. However, anyone that is not a member of the registry can request information by submitting an application to, and receiving authorization from, the Ministry of Magic. Information that will be requested from the registry will be name, mailing address and email address of those listed in this registry that reside in the US, specifically, the Mid-West.

**Data Safety Monitoring Board:** A data safety monitoring board has been established with the International Association for Data Monitoring, London UK, and Gryffindor Pty. Ltd. Adverse events will be tracked. If an unacceptable level of adverse events to subjects occurs, the study will be halted. DSMB will meet prior to the first subject being enrolled and then after the first 5 have completed the study. They will then meet once per quarter. They will also meet after each SAE is reported. Additional information can be found in the DSMB Charter. The study is expected to last about one year. The sponsor will submit annual reports to the IRB.

**Biospecimen Banking:** As the effects of QM-1 virus infection on the MuGL gene are not well understood, all participants must donate blood samples (10 ml) taken at the time of the initial protocol-specified blood sample, for DNA sequencing and various *in vitro* assays studying the interaction between QM-1 and MuGL gene. Additional blood (up to 10ml) will be collected and banked for future research related to QM-1, MuGL and Snapeacillium, or for other purposes. Samples will be stored at Gryffindor Pty, Ltd, and will be the sole property of that company. The DNA and other associated information will not be shared in the future with other researchers outside of Gryffindor Pty, Ltd. Information that will be stored with the samples include subject age at time of sample collection, MAS from first and last visits and diagnosis of Quidmort. No identifying information, or links to identifying information will be stored with the samples. Results of these tests are not shared with participants.

**Outcomes:** The primary outcome of the study is QM-1 viral load below the lower limit of detection (LLD) at Month 6. Secondary outcomes include 1) Change in viral load level from baseline to Month 6 and 2) The MAS score at Month 6.

**Data analysis:** The Boggart Banishing Spell (BBS) will be performed initially. The BBS will be used to analyze whether any magical skill has returned within the first month. If this analysis fails to show improvement in the magical skills, then the following spell analyses will be performed, in the listed order, until one has shown there has been an improvement in magical abilities:

1. Accio
2. Alhomora

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3. Crucio
4. Petrificus Totalus

**Power Analysis:** The study will randomize eligible patients in a 1:1 ratio of Snapeacillium to placebo. In order to conduct a safety assessment where an adverse event occurs at 5% or greater proportion with a 64% probability of observing an event, 20 treated patients will be needed. With 30 patients, the detection of an event rate of 5% will have a probability of 79%. If the true relative risk of adverse events for experimental subjects relative to controls is 3, with a study 30 experimental subjects and 30 control subjects we will be able to reject the null hypothesis if the baseline rate is 20% with probability (power) 0.9. The Type I error probability associated with this test of this null hypothesis is 0.05.

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