



PHARMACEUTICALS
(PTY)LTD

PRESS RELEASE

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Fast-acting herb set to revolutionise global stress-reduction market

A highly effective, fast-acting, mood-lifting and anxiety-reducing indigenous plant extract called Zembrin® has hit the complementary medicine shelves in South Africa, marketed locally as packs of Elev8 tablets.

The South African produced and patented Zembrin® is an extract of a cultivated elite selection of the Namaqualand plant *Sceletium tortuosum* - for centuries used and traded by San hunter-gatherers and Khoi Khoi pastoralists for medicinal, social and spiritual purposes. Zembrin® has been researched and developed for more than a decade and is presently being marketed in South Africa and the United States as a safe over-the-counter remedy for healthy people to enhance mood, decrease anxiety, and to reduce stress.

Zembrin® has been clinically tested for safety and efficacy in three rigorous placebo-controlled clinical studies. There is preliminary clinical evidence that the extracts effect, described by the excited researcher as “experiential”, which can be felt two hours after oral ingestion (versus up to two to three weeks with some well-known pharmaceutical anti-depressive drugs). This has huge global market potential. Prozac and newer mainstream drugs, such as Cymbalta and Effexor, are routinely provided to around 40 million patients by doctors in the United States and Europe for a wide variety of mood disorders including major depression, obsessive-compulsive disorder, anxiety and severe premenstrual syndrome. Zembrin®’s team of developers are however taking a conservative approach initially, by marketing Zembrin® for use in lower doses as health supplement products for people who are not clinically depressed or anxious.

HG&H Pharmaceuticals (Pty) Ltd, the research-based company that developed Zembrin®, is actively looking for a large pharmaceutical company to partner with for the development of higher dose products for registration as botanical medicines for the treatment of mental health diseases.

This development has taken place just as the United States Federal Drug Administration (FDA) approved its first-ever orally ingested botanical medicine, known as Crofelemer. The precedent-setting FDA registration is also the ultimate goal for HG&H Pharmaceuticals. Like Zembrin®, Crofelemer (trade name Fulyzaq) is a poly-molecular botanical medicine, but developed from the latex of an Amazonian tree. Crofelemer was approved in January by the FDA for the treatment of AIDS-related diarrhoea.

Developer’s excitement based on hard science

The Research and Development team’s excitement over Zembrin® is anything but hype. Already, an initial brain imaging study led by Professor Dan Stein, Head of the Department of Psychiatry and Mental Health at the University of Cape Town, shows that a single 25mg dose of Zembrin® has ‘effects on neural circuits involved in processing

emotions'. This study, due for peer review and publication later this year, focuses on activity in the amygdala and its connected neuro-circuitry and is characterised by Stein as; 'important in beginning to understand exactly how Zembrin® exerts its effects'. The full details of the study will be released in due course. Two earlier randomized, double-blind studies with groups of healthy adults, one in Cape Town and the other in Canada, show Zembrin® to be safe and well-tolerated. The first study, purely a safety study, reported unsolicited positive effects on wellbeing, including improved coping with stress and enhanced sleep in subjects taking once-daily doses continually for three months. The second study, presented at the World Psychiatric Association Congress in Prague in 2012, concluded that Zembrin® significantly improved cognitive flexibility and executive function, suggesting that the extract may also have therapeutic potential in cognitive ageing. The Canadian clinical investigators believe that Zembrin® should be studied as a treatment for neurodegenerative disorders, including Alzheimer's disease.

Elev8 tablets containing 25mg Zembrin® were approved for sale as complementary medicine by the South African Medicines Control Council (MCC) in June last year, and have been available through most pharmacies since September 2012.

In March 2013, Zembrin® was recognised as the 'most sustainable ingredient' at the prestigious annual Natural Products Expo West held in Anaheim, USA. Zembrin was noted as one of the leading ingredients pioneering the next great foundation of new product development.

Self-care for 'those not seeing a psychiatrist'

South African medical practitioner, botanist and ethnopharmacologist Dr Nigel Gericke together with Deon Hofmeyr, a horticulturalist and entrepreneur, with backing from H.L. Hall and Sons, developed Zembrin® by directing an international multidisciplinary team effort. According to Gericke 'For now we're promoting the use of Zembrin® as a botanical supplement for self-medication for healthy people suffering from stress, low mood and mild anxiety, who need a clinically studied product with a rapid onset of tangible activity. However, our pharmacological research and clinical studies have been so encouraging that we believe Zembrin® has the potential to be developed into a blockbuster botanical medicine for treating serious mental health conditions, which meets a need for a rapidly acting, safe, effective, natural medicine'.

Gericke came across Sceletium in 1986 during a gap year after his medical studies when he read a book in Australia on psychoactive plants from around the world. There was a brief mention of an obscure South African plant called Sceletium without much known about its effect – which he found intriguing, and determined to investigate on his return home. Gericke and a small group of friends consisting of ethnobotanists, doctors and psychiatrists then experimented with various doses of the plant. It was immediately apparent that low doses of the plant had a subtle effect, providing 'a sense of alert serenity,' while excessive doses caused a transient euphoria. These observations and comparisons with the side-effects of high doses with those of mainstream anti-depressives made by Gericke's psychiatrist wife Olga, ultimately led them to confirm that some of the plant's compounds are potent serotonin re-uptake inhibitors (Prozac-like activity). The research team then hunted for an explanation for the surprisingly rapid onset of action, finally discovering that Zembrin® is also a potent PDE4 inhibitor, a very current research target of pharmaceutical companies for treating anxiety, depression and neurodegenerative diseases such as Alzheimer's disease.

Addictive potential ruled out

To evaluate possible addictive effects at the outset of the project, in 1995 Dr Gericke took one of the country’s leading addiction specialists at the time, psychiatrist Dr Greg McCarthy, with him on a field trip to the Namaqualand villages of Paulshoek and Nourivier to interview local people about the use of Sceletium, known locally as “kougoed” and to evaluate additional potential. McCarthy, (who rehabilitated drug addicts in Cape Town) and Gericke interviewed many elders and shepherds from the community, some of whom had been using the plant on a daily basis for over 40 years and found them to be ‘in perfect health’. Gericke noted that elderly Sceletium users were surprisingly lucid in spite of advanced age. McCarthy was unable to find any folk who were socially dysfunctional as a result of Sceletium use.

Social responsibility

The Zembrin® founders are also the first local developmental entrepreneurs to sign Africa’s first “prior informed consent benefit-sharing agreement” with a South African indigenous community. In terms of this agreement they will share six percent of all income from Zembrin® with the San Council which generously agreed, and formalized, to allocate 50% of their share with the villagers of Paulshoek and Nourivier. The villagers’ input on what plants to use, doses, and participation in the addiction study were pivotal to the initial research and development on Zembrin®.

Quipped Dr Roger Chennels, a veteran human rights lawyer and San expert who brokered the deals, ‘when something’s been tested for over 10 000 years, it really works. We all chewed it during our negotiations which led to things going very smoothly and a happy outcome’.

All the raw plant material for Zembrin® comes from 10 hectares of Sceletium grown outside Nelspruit, (half under shade cloth and half on open land) belonging to the company’s major shareholders, HL Hall and Sons. Another large tranche comes from a huge fruit farming operation near Tzaneen.

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