Terbinafine topical - Celtic Pharma

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As of May 2015, no recent reports of development for topical terbinafine (TDT 067) have been identified for the treatment of onychomycosis. The product was under phase III development with Celtic Pharma in the US, Germany and Iceland. The product was the lead compound in a research programme originally created by IDEA AG. TDT 067 (IDEA 067) contains the anti-fungal drug terbinafine and utilises IDEA AG's proprietary Transfersome ®drug delivery technology. Transfersomes ®are bio-compatible, highly deformable, self-regulating, water-based vesicles, which are used to transport established, low molecular weight drugs selectively into the skin and in the immediately adjacent underlying tissues.

COMPANY AGREEMENTS

In February 2006, Celtic Pharma acquired worldwide rights to topical terbinafine, following the acquisition of an exclusive global license to IDEA's Transfersome ®drug delivery technology (Reference: 809061326).

KEY DEVELOPMENT MILESTONES

As of May 2015, no recent reports of development for topical terbinafine have been identified for the treatment of onychomycosis.

Celtic Pharma initiated a randomised, double-blind, vehicle- and placebo-controlled phase III trial in April 2010, to assess the efficacy and safety of topical terbinafine 1.5% in patients with mild to moderate distal subungual onychomycosis of the toenails (NCT01145807; EudraCT 2010-018793-21; CL-067-III-01). Treatment was applied twice-daily for 48 weeks, and the primary endpoint was cure rate at 52 weeks. The trial enrolled 738 patients in the US, Germany and Iceland, and was completed in January 2012. Celtic Pharma appointed PPD Inc., a global contract research organisation, to conduct the study (Reference: 809111963) (Reference: 700244950).

Celtic Pharma initiated a randomised, crossover phase II trial in December 2009, to establish a clinical bridge between topical terbinafine and terbinafine oral tablets (Lamisil ®) in patients with distal subungual onychomycosis of the toenails (NCT01790165). The aim of the trial was to confirm that treatment with topical terbinafine is associated with significantly lower plasma levels of terbinafine, than the oral formulation. The trial enrolled 27 patients in the US, and was completed in June 2012 (Reference: 700244953).

In June 2008, Celtic Pharma enrolled the first patient into a phase II trial, designed to assess the efficacy and safety of topical terbinafine (Reference: 809090275). The trial was completed and results were reported in March 2009 (Reference: 809110799).

At the BioSquare-2005 meeting, IDEA announced that topical terbinafine was undergoing further research for the treatment onychomycosis (Reference: 801009169).

Data from two *in vitro* studies of TDT 067 were reported in February 2011 (Reference: 809121232).

Adverse Event

TDT 067 was well tolerated in a phase II trial in patients with onychomycosis. Systemic drug exposure was negligible; no patient had >2 ng/mL of terbinafine at steady state and majority of patients had levels below 1 ng/mL. No serious local side effects were reported (Reference: 809110799).

Pharmacokinetics

In a pharmacokinetic study, maximally used TDT 067 achieved two orders of magnitude lower plasma concentrations of terbinafine compared with oral terbinafine. In contrast, terbinafine levels in affected nails were three orders of magnitude higher compared with oral terbinafine (Reference: 809111963).

Pharmacodynamics

Mycoses

TDT 067 was shown *in vitro* to have potent inhibitory and fungicidal activity against dermatophyte strains. Data also demonstrated that TDT 067 has more potent fungicidal activity than conventional terbinafine preparations. In another *in vitro* study, the terbinafine formulated in transfersomes in TDT 067 was shown to potentiate the action of terbinafine by enabling it to penetrate more effectively to its site of action inside the fungus, disrupting the intracellular matrix and eventually killing dermatophyte hyphae (Reference: 809121232).

Therapeutic Trials

Mycoses

Treatment with TDT 067 resulted in 90% negative mycological cure rate at 14 weeks in a phase II trial in patients with onychomycosis. At 48 weeks, the mycological cure rate was 38%. In the study, patients were treated with TDT 067 for 12 weeks and the primary endpoint of mycological cure was measured at 14 weeks and 48 weeks (Reference: 809110799).

Pharmacodynamics

More potent *in vitro* than conventional terbinafine preparations

References

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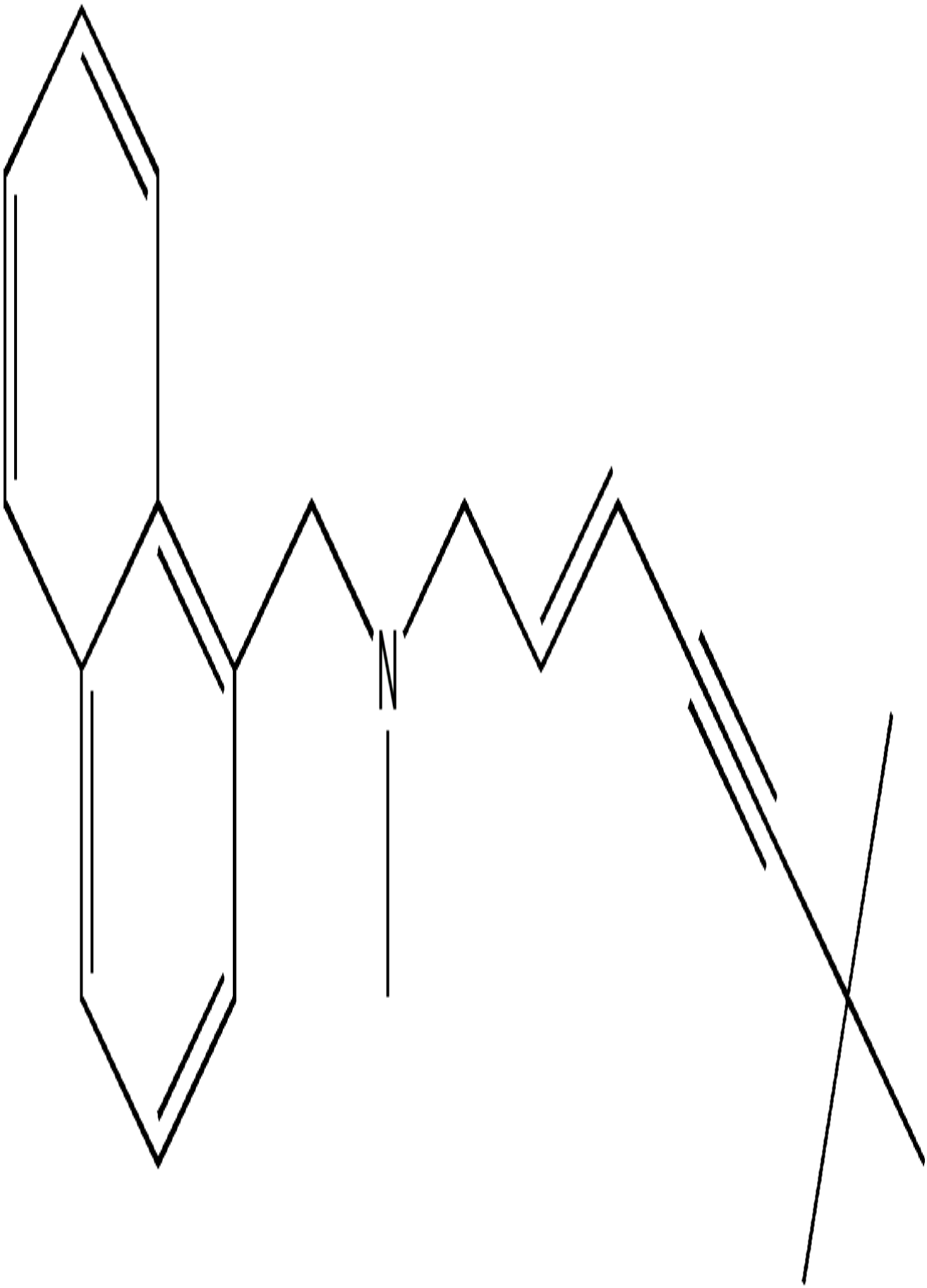

History of Drug Development

Event date	Update date	Update type	Significant	Details
20040615	20040701	Phase Change	true	Preclinical trials in Onychomycosis in Germany (unspecified route)
20040701	20040701	New Profile	true	Profile created from data presented at the BIO 2004 International Annual Convention (BIO-2004)
20060223	20060316	Licensing Status	true	IDEA 067 has been licensed to Celtic Pharma worldwide
20071015	20080620	Phase Change	false	Phase-II clinical trials in Onychomycosis in USA (Topical)
20090326	20100325	Scientific Update	false	Efficacy and safety data from a phase II trial in Onychomycosis released by Celtic Pharma (9110799)
20090326	20100827	Trial Update	false	Celtic Pharma completes a phase-II trial in Onychomycosis in USA (Topical)
20091231	20130226	Trial Update	true	Celtic Pharma initiates enrolment in a phase II trial for Onychomycosis in USA (NCT01790165)
20100430	20100503	Phase Change	true	Phase-III clinical trials in Onychomycosis in USA (Topical)
20100503	20100503	Scientific Update	true	Pharmacokinetic data from a phase II trial in Onychomycosis released by Celtic Pharma (9111963)
20100505	20130226	Phase Change	true	Phase-III clinical trials in Onychomycosis in Iceland (Topical)
20100505	20130226	Phase Change	true	Phase-III clinical trials in Onychomycosis in Germany (Topical)
20110208	20110209	Scientific Update	true	Pharmacodynamics data from in vitro studies in Onychomycosis presented at the 69th Annual Meeting of the American Academy of Dermatology (AAD-2011) (9121232)
201201	2013022			Celtic Pharma completes a phase III trial in Onychomycosis

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