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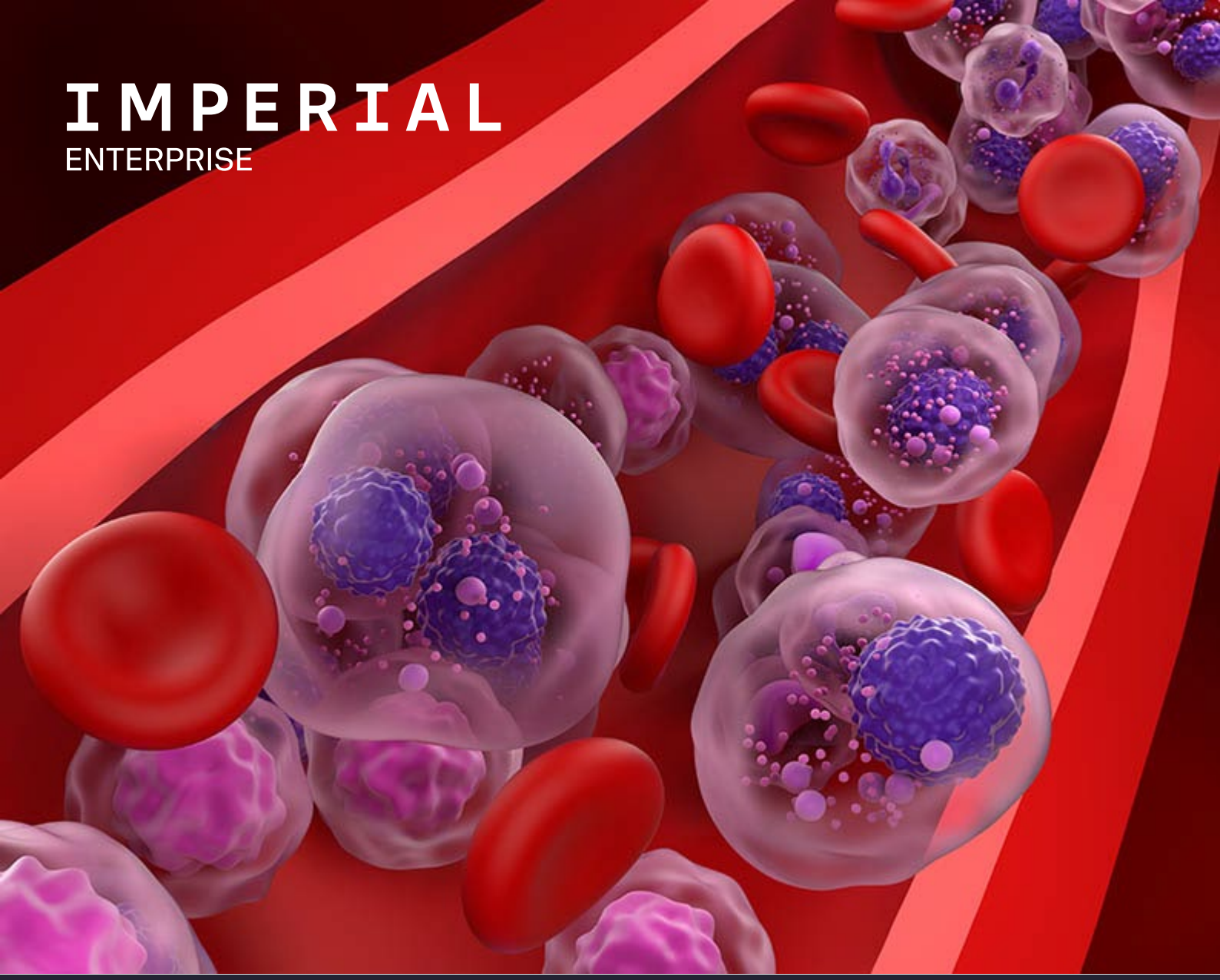

First-in-class therapeutic for the treatment of Multiple Myeloma with opportunity in other cancers

DTP3 is a first-in-class GADD45β/MKK7 inhibitor selectively targeting the NF-κB pathway in cancer cells, with applications in Multiple Myeloma (MM), Diffuse Large B-Cell Lymphoma (DLBCL) and development opportunities in other cancers.

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Technology reference: 4780, 5678, 6324

Intellectual property information

WO2011048390A2 – Gadd45beta targeting agents (composition of matter + methods of use)

WO2012146940 – Gadd45beta as an expression marker useful for the diagnosis, prognosis and theranostics of cancer

Inventor information

Professor Guido Franzoso

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Proposed Uses

MM cells are addicted to an aberrant NF-κB activity for survival and therapy resistance. By disrupting the essential GADD45β/MKK7 survival complex downstream of NF-κB, DTP3 induces JNK-mediated apoptosis selectively in MM cells, whilst leaving healthy cells unharmed, to provide an effective and non-toxic drug solution.

DTP3's enhanced tolerability and ability to bypass drug resistance makes it a promising candidate as a salvage therapy in patients with relapsed or refractory MM. Subsequently, DTP3 is envisaged forming part of an earlier-line/frontline polytherapy in combination with other agents, exploiting its synergistic activity and benign safety profile. Secondary indications include DLBCL and other cancers in which NF-κB promotes malignant cell survival via GADD45β/MKK7.

Problem addressed

Despite the introduction of new therapies, MM remains incurable, with a median survival of about 5 years. Nearly all patients eventually relapse and develop resistance to existing treatments. As a result, the 10-year survival for MM is amongst the lowest of the 20 most common cancers. Given the lack of permanent solutions and adverse effects of many existing treatments, safer and mechanistically novel therapies are urgently needed to improve the outcomes of MM patients.

The NF-κB pathway has been aggressively pursued as an effective therapeutic target in MM and other cancers. Yet, developing clinically useful NF-κB inhibitors has proven impossible, due to systemic on-target toxicities. DTP3 overcomes this problem by targeting the cancer-restricted, GADD45β/MKK7 survival module downstream of NF-κB, rather than NF-κB itself. Owing to this unique mode of action (MoA), DTP3 selectively blocks NF-κB-dependent survival in MM cells without toxicity to normal tissues.

Technology Overview

DTP3 is a D-tripeptide that specifically binds to the JNK kinase, MKK7, with high affinity to disrupts its interaction with the NF-κB-dependent anti-apoptotic effector, GADD45β, and restore MKK7 catalytic activity. As a result, DTP3 selectively induces spontaneous JNK-mediated apoptosis in MM cells without affecting NF-κB's physiological functions or harming healthy tissues.

A completed dose-escalation phase (Phase I) has shown a lack of toxicity at DTP3 doses that demonstrate clear clinical efficacy (e.g., Very Good Partial Response) in heavily pre-treated patients (4-11 previous lines of therapy). DTP3 also triggered cancer-selective pharmacodynamic responses in about 50% of patients, with activation of JNK-mediated apoptosis in MM cells and no drug-related responses in normal cells. The trial entered its dose-expansion phase (Phase II) in October 2025.

Inventor information

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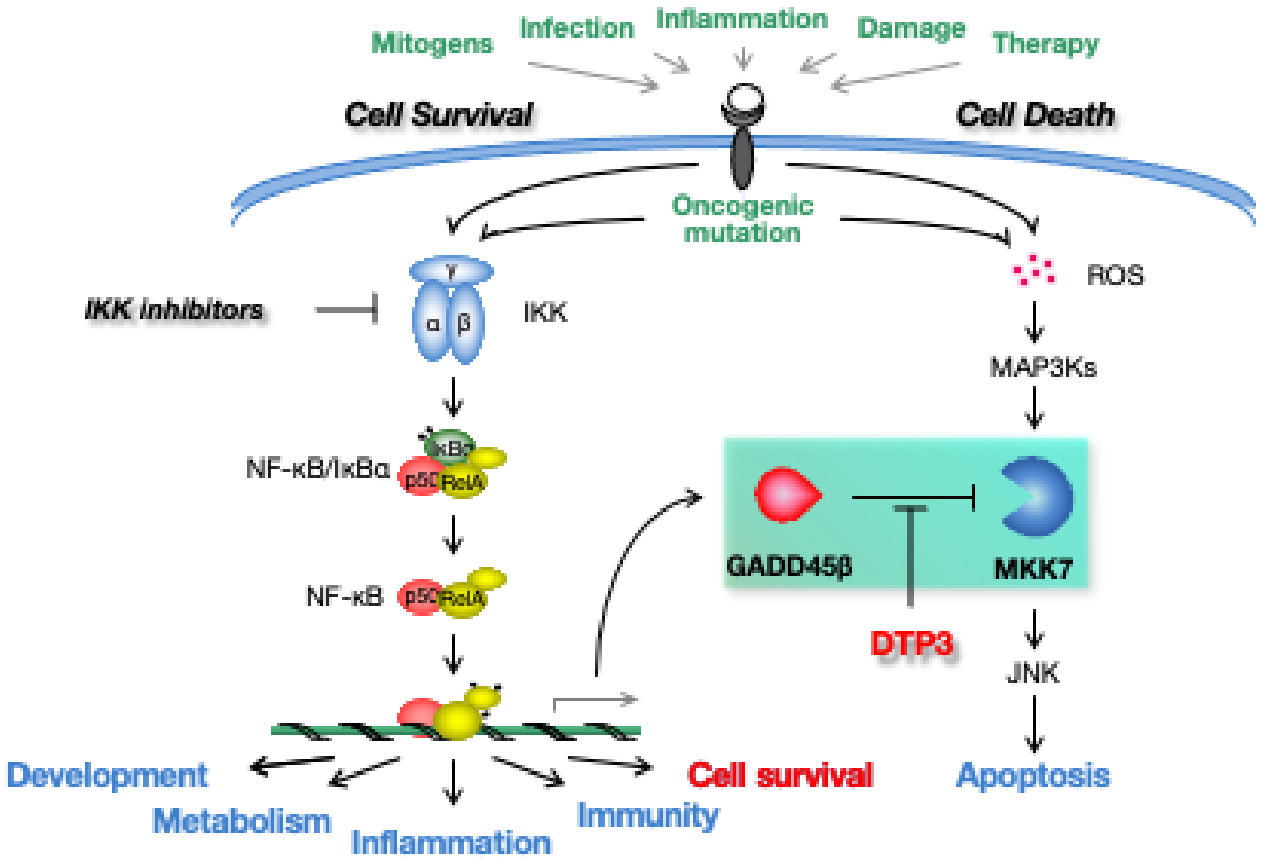
Benefits

- Unique MoA selectively targeting the NF-κB pathway in cancer cells
- Selectively induces JNK-mediated apoptosis in MM and other cancer cells
- High on-target selective specificity in vitro and in vivo
- Similar potency to the clinical standard, bortezomib, but a more than 100 times wider therapeutic index ex vivo and far greater tolerability in vivo
- High tolerability with no toxicity at therapeutically effective doses in animal models and humans
- Ability to bypass resistance to multiple drug classes routinely used in MM and DLBCL
- Synergistic activity with standard-of-care agents in MM
- Predictive biomarkers identified, with companion diagnostics for patient stratification in development



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Publications

11/2025, *Blood* – Cancer-selective targeting of the NF-κB pathway via GADD45β/MKK7 inhibition: Results from the phase I trial of the first-in-class inhibitor, DTP3, in patients with relapsed or refractory multiple myeloma

09/2022, *Biomedicines* – The NF-κB pharmacopeia: novel strategies to subdue an intractable target

12/2020, *Biomedicines* – Insights into the Interaction Mechanism of DTP3 with MKK7 by Using STD-NMR and Computational Approaches

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09/2018, *British Journal of Haematology* – Clinical proof of concept for a safe and effective NF-κB-targeting strategy in multiple myeloma

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12/2015, *Blood* – Cancer-Selective Targeting of the NF-κB Survival Pathway in Multiple Myeloma with the GADD45β/MKK7 Inhibitor, DTP3

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