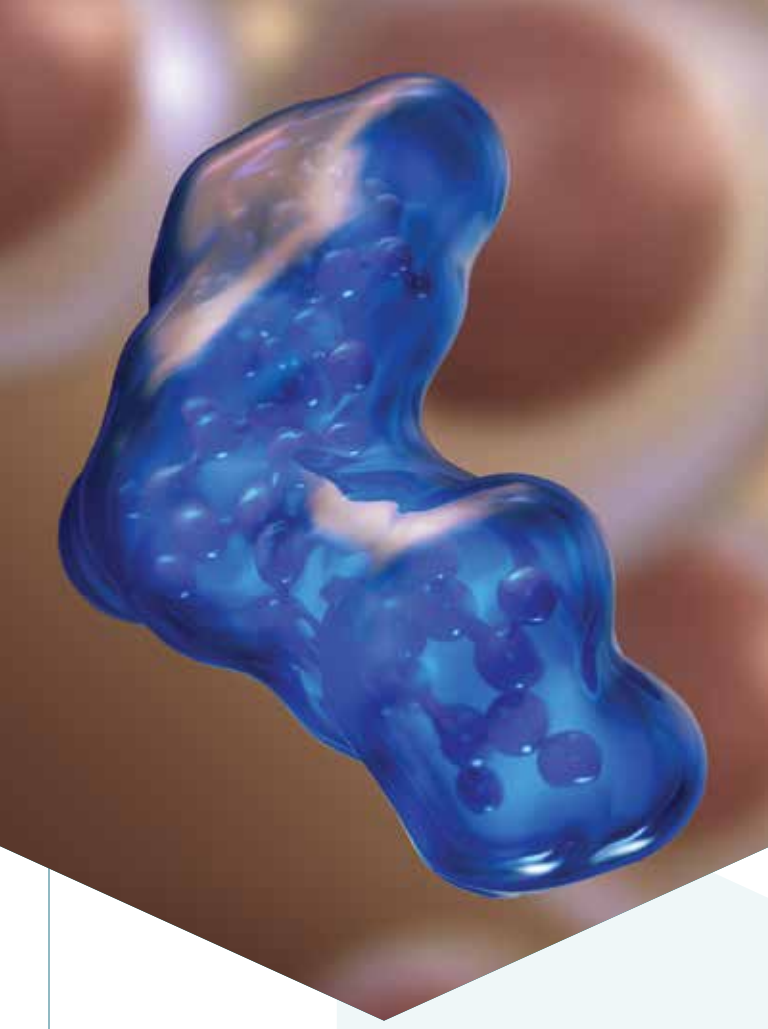


Filanesib (ARRY-520)

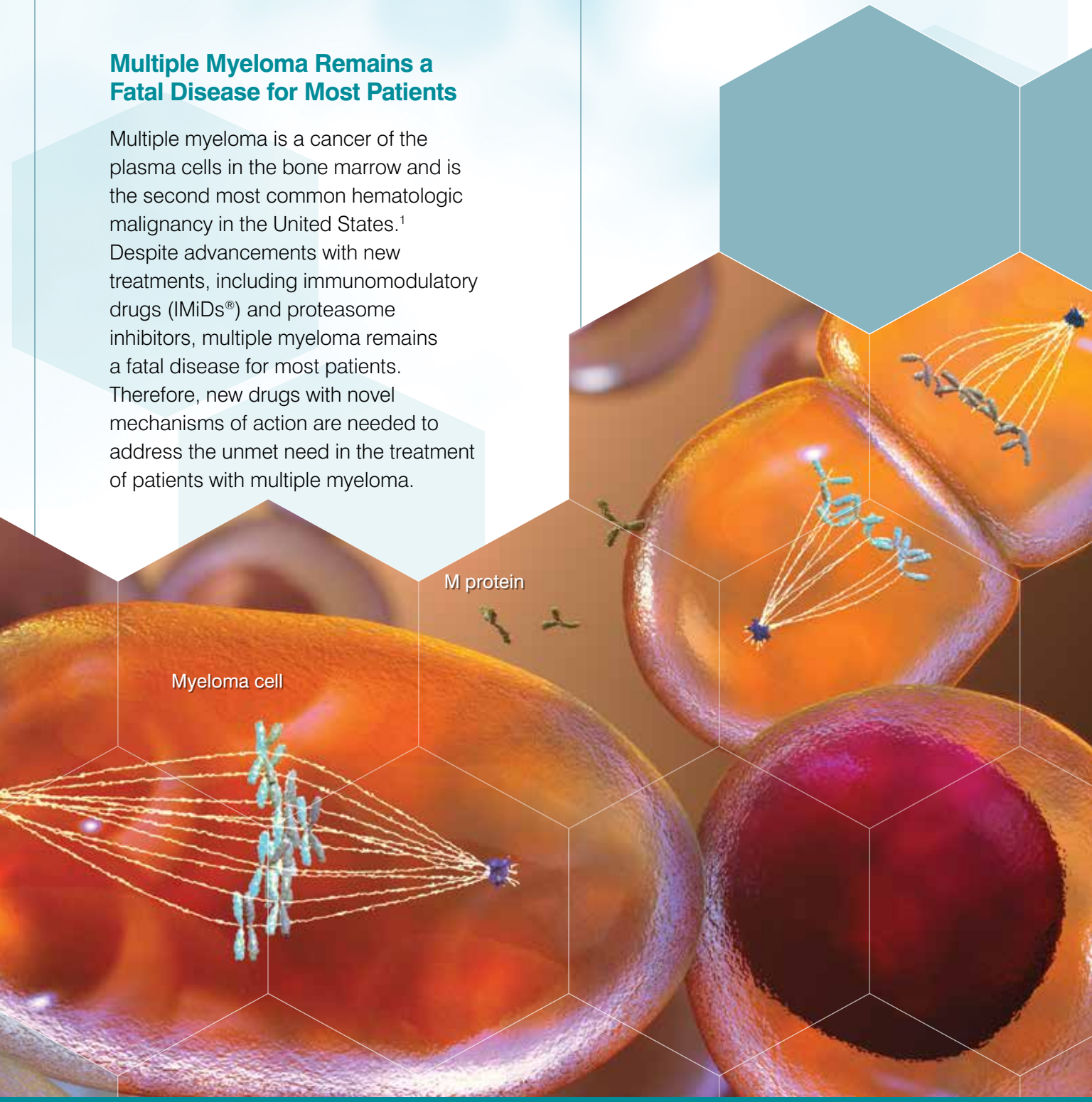
TARGETED KSP INHIBITION

A Novel Approach to the Treatment of Patients With Multiple Myeloma

ARRAY BIOPHARMA

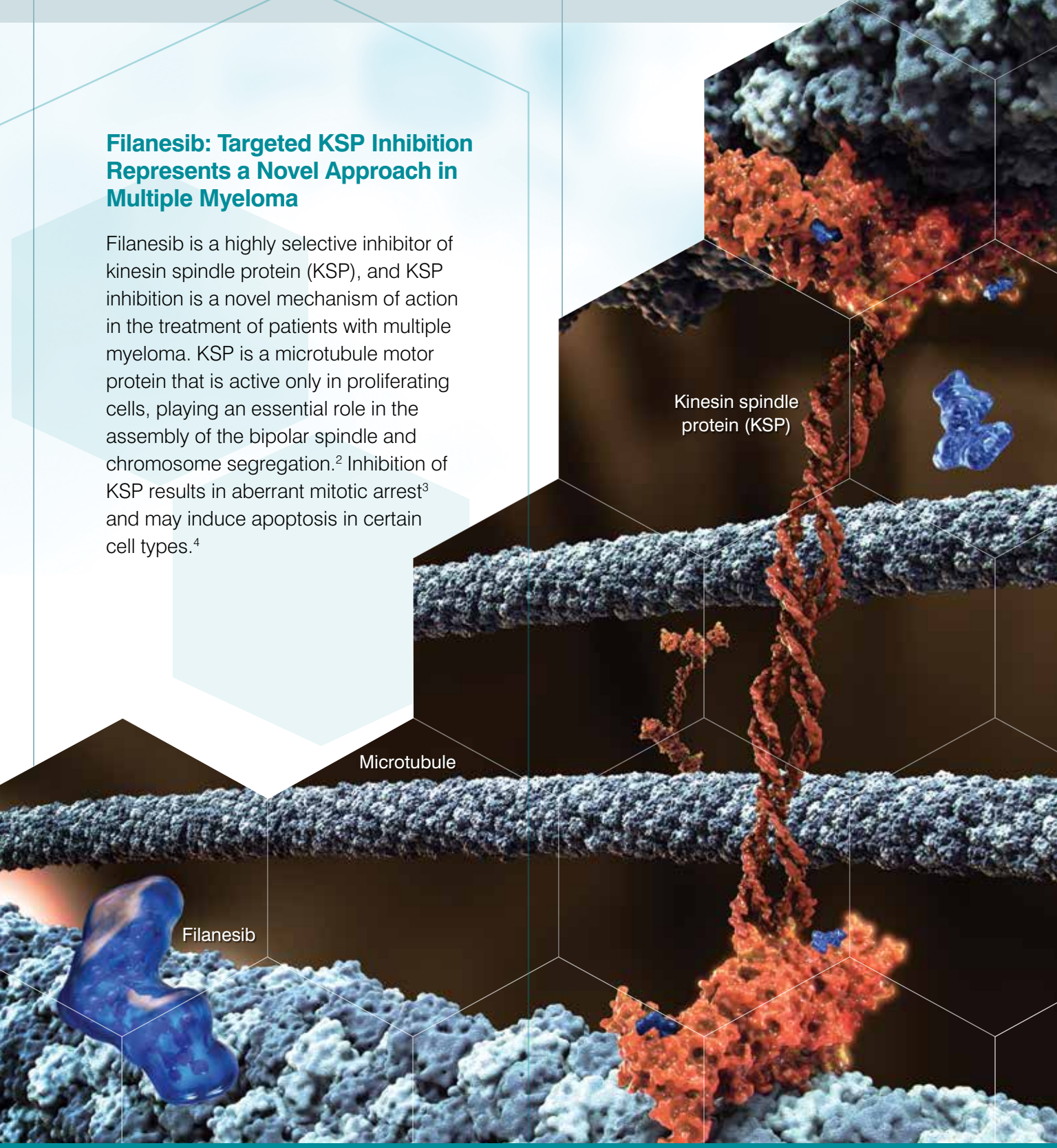
Multiple Myeloma Remains a Fatal Disease for Most Patients

Multiple myeloma is a cancer of the plasma cells in the bone marrow and is the second most common hematologic malignancy in the United States.[1] Despite advancements with new treatments, including immunomodulatory drugs (IMiDs®) and proteasome inhibitors, multiple myeloma remains a fatal disease for most patients. Therefore, new drugs with novel mechanisms of action are needed to address the unmet need in the treatment of patients with multiple myeloma.



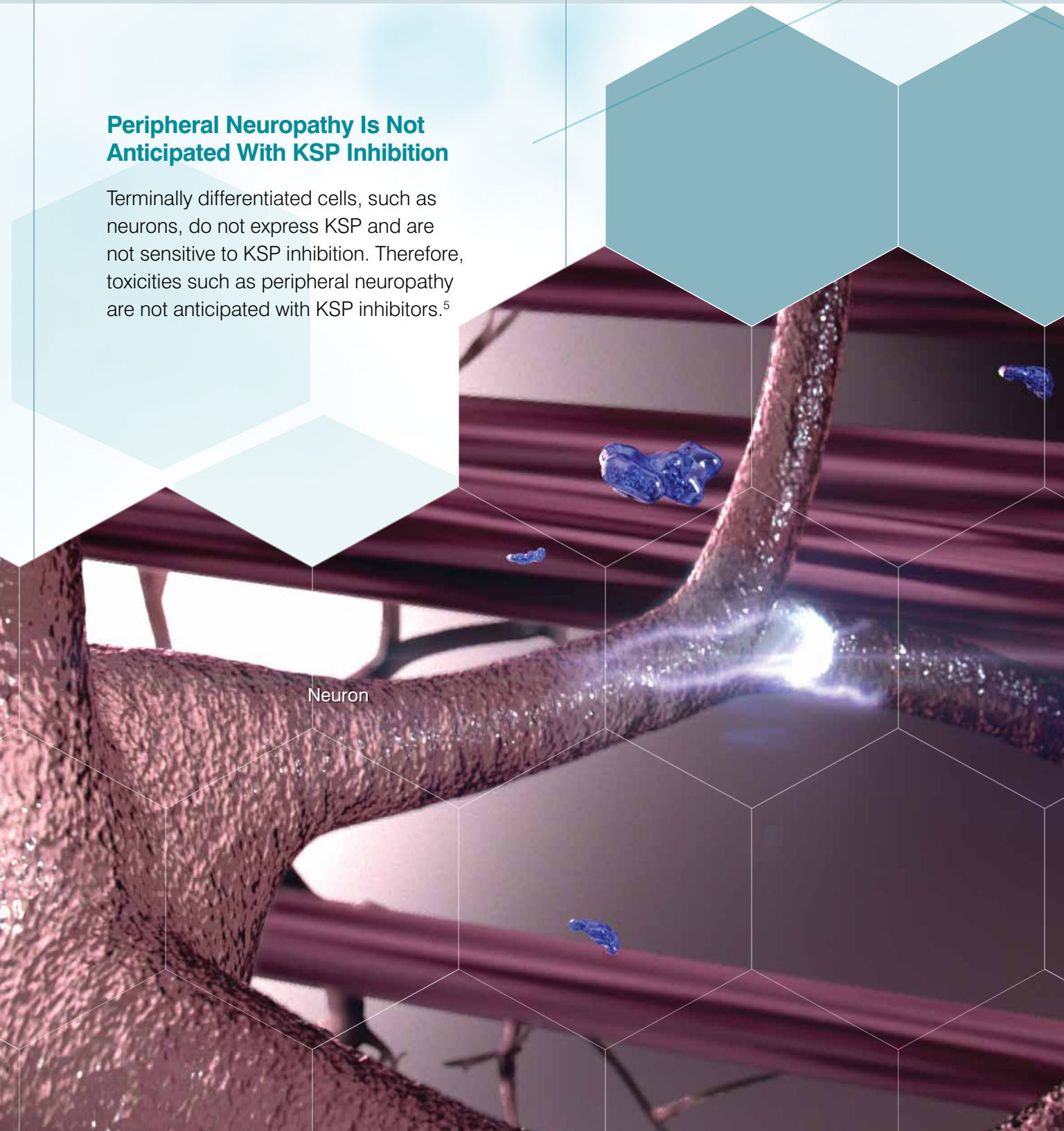
Filanesib: Targeted KSP Inhibition Represents a Novel Approach in Multiple Myeloma

Filanesib is a highly selective inhibitor of kinesin spindle protein (KSP), and KSP inhibition is a novel mechanism of action in the treatment of patients with multiple myeloma. KSP is a microtubule motor protein that is active only in proliferating cells, playing an essential role in the assembly of the bipolar spindle and chromosome segregation.[2] Inhibition of KSP results in aberrant mitotic arrest[3] and may induce apoptosis in certain cell types.[4]



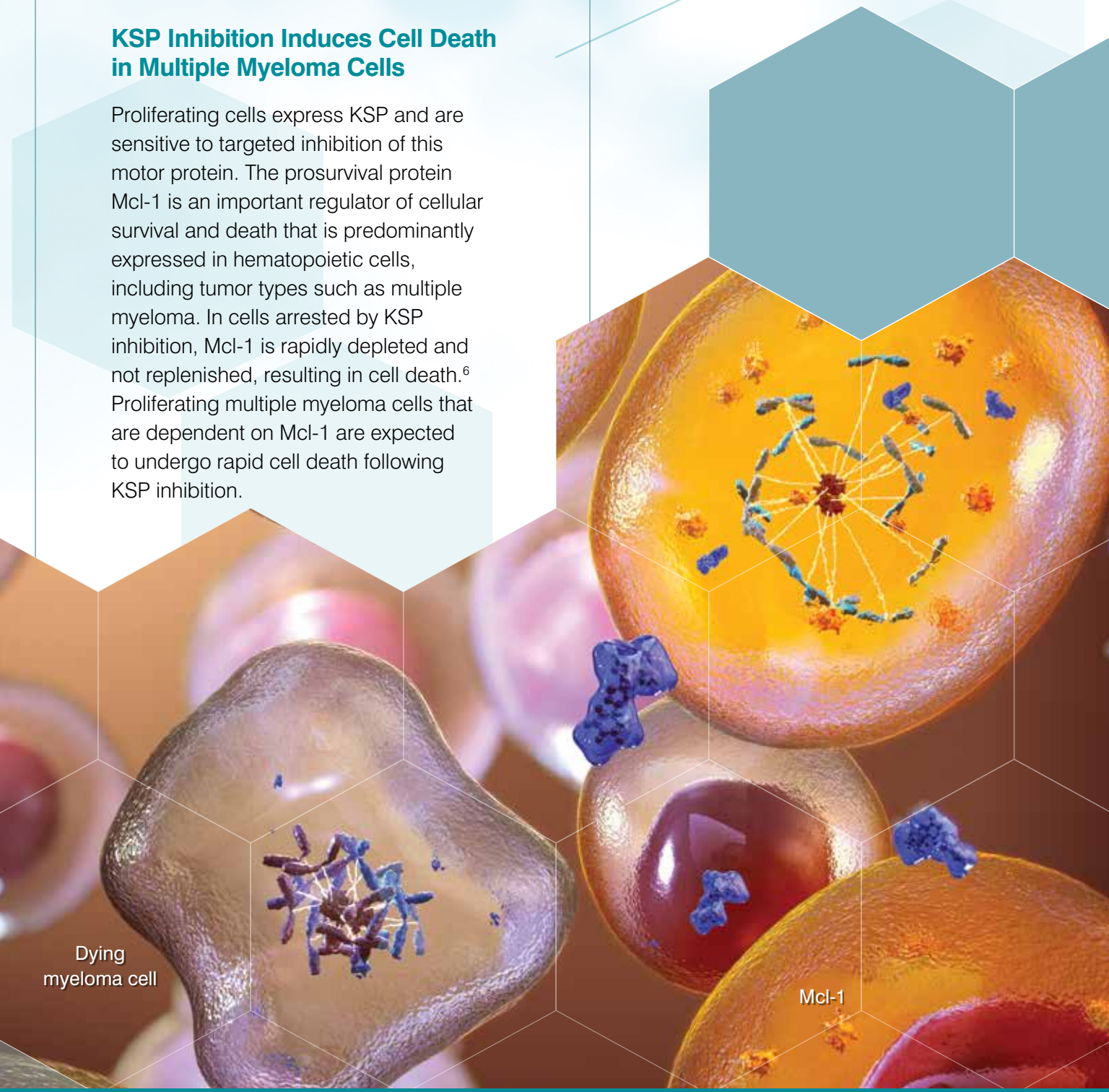
Peripheral Neuropathy Is Not Anticipated With KSP Inhibition

Terminally differentiated cells, such as neurons, do not express KSP and are not sensitive to KSP inhibition. Therefore, toxicities such as peripheral neuropathy are not anticipated with KSP inhibitors.[5]



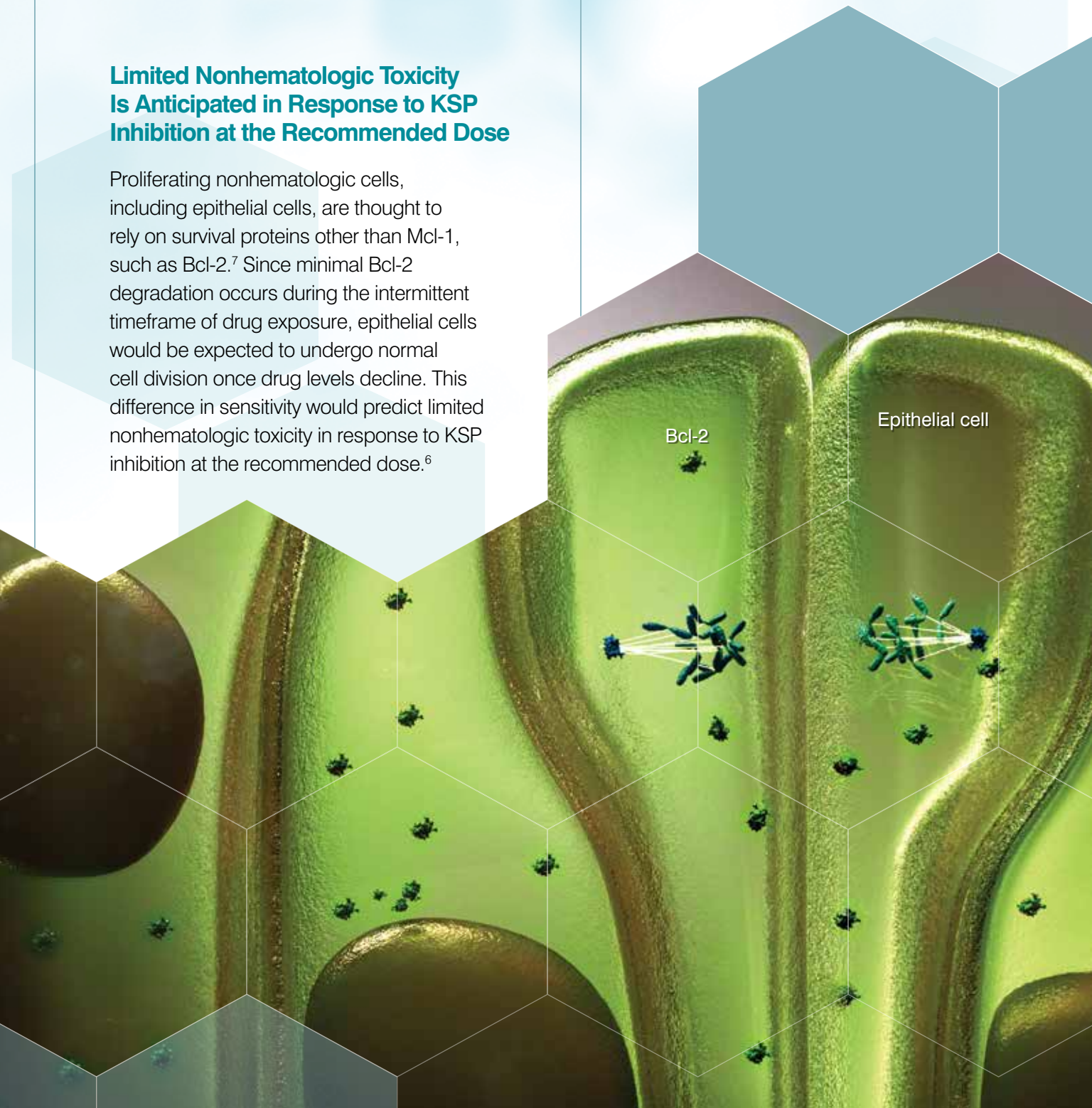
KSP Inhibition Induces Cell Death in Multiple Myeloma Cells

Proliferating cells express KSP and are sensitive to targeted inhibition of this motor protein. The prosurvival protein Mcl-1 is an important regulator of cellular survival and death that is predominantly expressed in hematopoietic cells, including tumor types such as multiple myeloma. In cells arrested by KSP inhibition, Mcl-1 is rapidly depleted and not replenished, resulting in cell death.[6] Proliferating multiple myeloma cells that are dependent on Mcl-1 are expected to undergo rapid cell death following KSP inhibition.



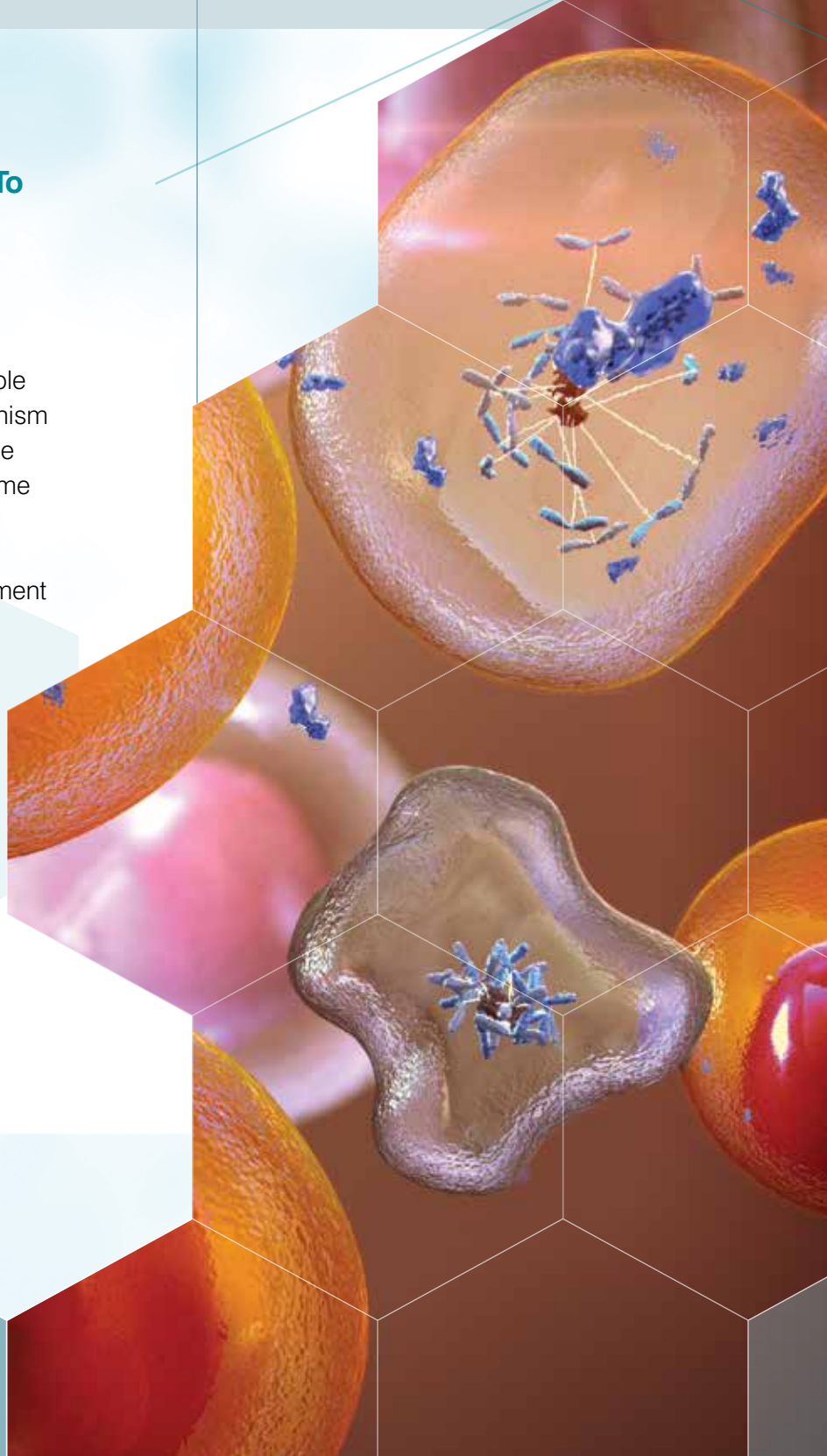
Limited Nonhematologic Toxicity Is Anticipated in Response to KSP Inhibition at the Recommended Dose

Proliferating nonhematologic cells, including epithelial cells, are thought to rely on survival proteins other than Mcl-1, such as Bcl-2.[7] Since minimal Bcl-2 degradation occurs during the intermittent timeframe of drug exposure, epithelial cells would be expected to undergo normal cell division once drug levels decline. This difference in sensitivity would predict limited nonhematologic toxicity in response to KSP inhibition at the recommended dose.[6]



KSP Inhibition Is Expected To Be Active in Myeloma Cells Refractory to Approved Myeloma Therapies

KSP inhibition represents a novel approach to the treatment of multiple myeloma. Due to a distinct mechanism of action, filanesib is expected to be active even in cells that have become resistant to IMiDs and proteasome inhibitors, potentially addressing a significant unmet need in the treatment of patients with multiple myeloma. Preclinically, filanesib has demonstrated additivity and synergy with IMiDs and proteasome inhibitors. Based on this scientific rationale, Array BioPharma Inc. is developing filanesib for patients with multiple myeloma as a monotherapy and in combination with proteasome inhibitors and other myeloma therapies.



About Array BioPharma Inc.

Array BioPharma Inc. is a biopharmaceutical company focused on the discovery, development, and commercialization of targeted small molecule drugs to treat cancer patients. Array is evolving into a late-stage-development company, with two wholly owned hematology programs, and two partnered MEK inhibitor programs currently enrolling patients in multiple registration trials in a variety of solid tumors.

Array is internally developing two product candidates in the oncology pipeline:

- **Filanesib (ARRY-520)** is a KSP inhibitor being developed to treat multiple myeloma. Filanesib has demonstrated activity both as a single agent and when combined with Kyprolis® (carfilzomib) and Velcade® (bortezomib). **Planned studies include a Phase 3 trial in combination with Kyprolis and a Phase 2 single-agent trial.**
- **ARRY-614** is an oral p38/Tie2 inhibitor with a novel mechanism of action being developed to treat myelodysplastic syndromes (MDS).

MEK inhibitor programs include selumetinib, partnered with AstraZeneca, and MEK162, in collaboration with Novartis.

References

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Filanesib (ARRY-520)

TARGETED KSP INHIBITION

- Multiple myeloma remains a fatal disease for most patients
- Targeted KSP inhibition induces cell death in multiple myeloma cells, representing a novel approach to the treatment of multiple myeloma
- Peripheral neuropathy is not anticipated with KSP inhibition
- Limited nonhematologic toxicity is anticipated in response to KSP inhibition at the recommended dose
- KSP inhibition is expected to be active in myeloma cells refractory to proteasome inhibitors and IMiDs, potentially addressing a significant unmet need
- A potential patient selection marker, alpha-1 acid glycoprotein (AAG) is under investigation in ongoing filanesib clinical trials
- **Array BioPharma Inc.** is developing filanesib for patients with multiple myeloma in combination with proteasome inhibitors and as monotherapy

To view the filanesib MOA video, please scan the QR code on the left.

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