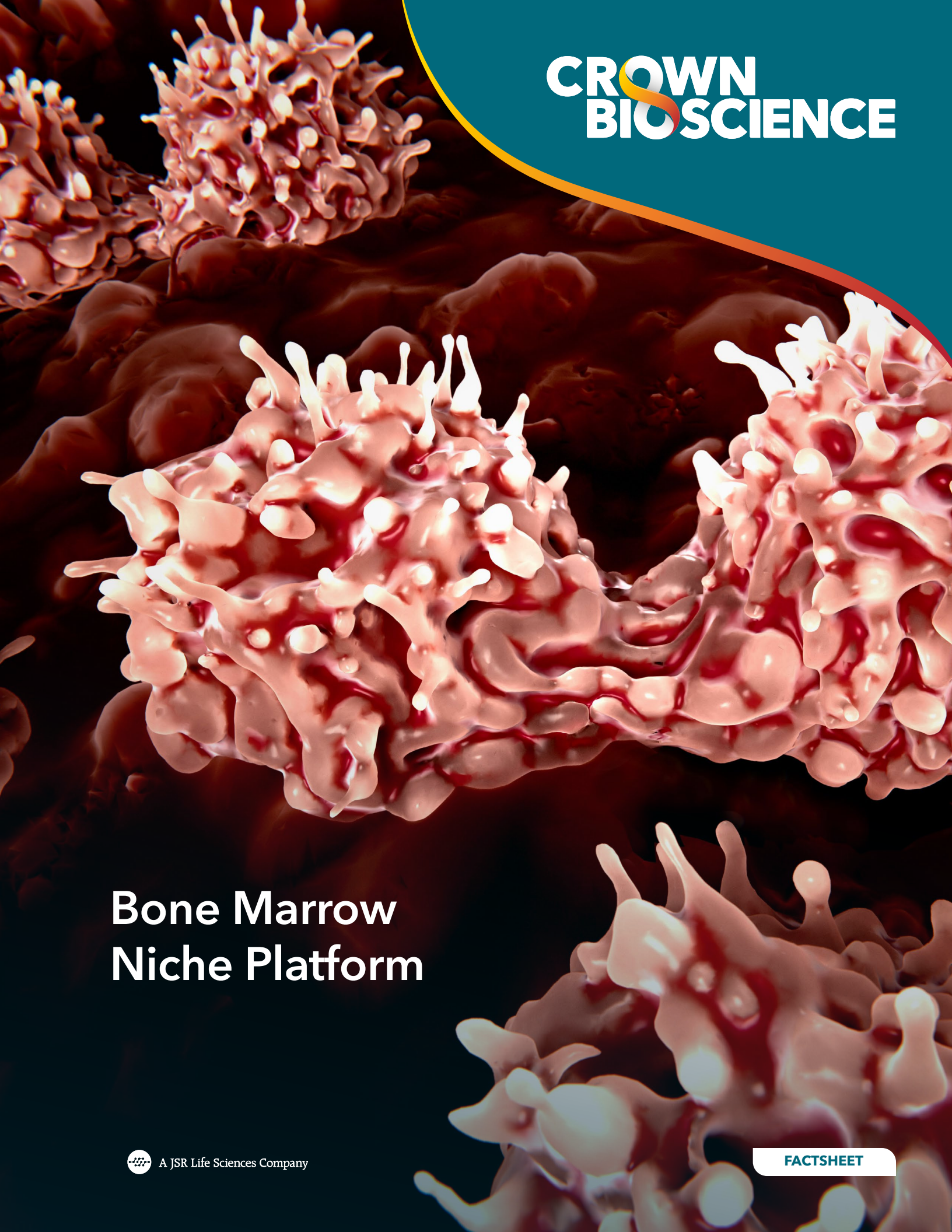
CROWN BIOSCIENCE



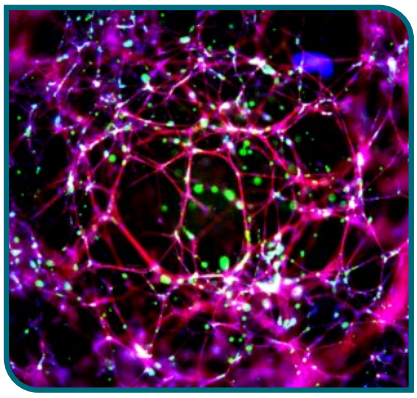
Bone Marrow Niche Platform

A JSR Life Sciences Company

FACTSHEET

Unlock the Power of 3D Bone Marrow Niche Models

At Crown Bioscience, we provide cutting-edge 3D bone marrow niche (BMN) *in vitro* models to advance hematological cancer research. These models accurately recapitulate the tumor microenvironment, offering a physiologically relevant system to study tumor progression, drug response, and immune interactions.



- **Clinically Relevant Tumor Modeling** – Assay therapy response in a physiologically relevant platform where patient-derived tumor cells proliferate, mimicking *in vivo* behavior.
- **Enhanced Translational Insights** – Leverage multi-modal analysis, including advanced imaging, to identify clinically relevant biomarkers and assess niche response for potential off-target effects.
- **Accelerated & Scalable Drug Testing** – Achieve faster timelines and higher throughput than *in vivo* models, with the potential to pre-screen PDX models *in vitro*.
- **Expanded Capabilities for Immuno-Oncology (IO) Studies** – Explore IO applications with the ability to incorporate immune components for a more comprehensive assessment.
- **Access to High-Quality Patient-Derived Material** – Utilize well-characterized tissue banks to support follow-up studies and deepen understanding of promising therapeutic leads.

Revolutionize Your Research with the Right Microenvironment

Breakthrough discoveries start with a strong foundation. Our 3D bone marrow niche models replicate the complexity of the human bone marrow to give you more reliable and predictive results.

Cellular Composition
A dynamic mix of hematopoietic stem and progenitor cells, stromal cells, endothelial, and immune cells for a lifelike research environment

Mechanical & Biophysical Cues
Fine-tuned stiffness, matrix composition, and signaling cues to mimic the dynamic nature of the bone marrow niche.

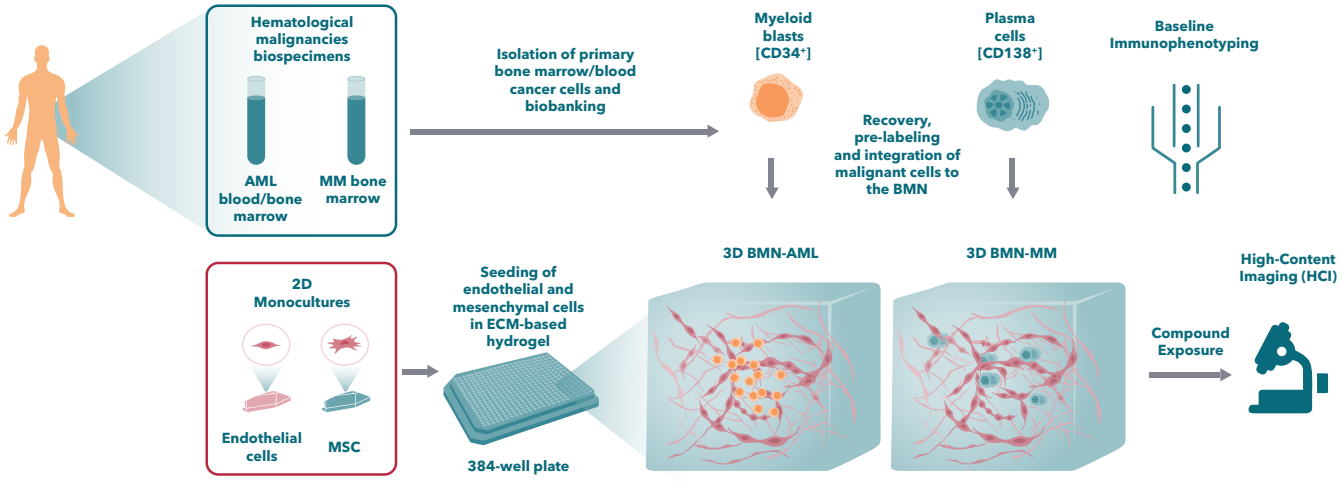
Pre-vascularization
Mesenchymal and endothelial cells form networks that contain key characteristics of pre-vascularization.

Optimized Structural Support
Engineered scaffolds that provide a physiologically relevant 3D architecture for enhanced cell adhesion and function.

Niche Critical Growth Factors
Physiologically relevant growth factors that enhance cell signaling paracrine action and disease modeling.

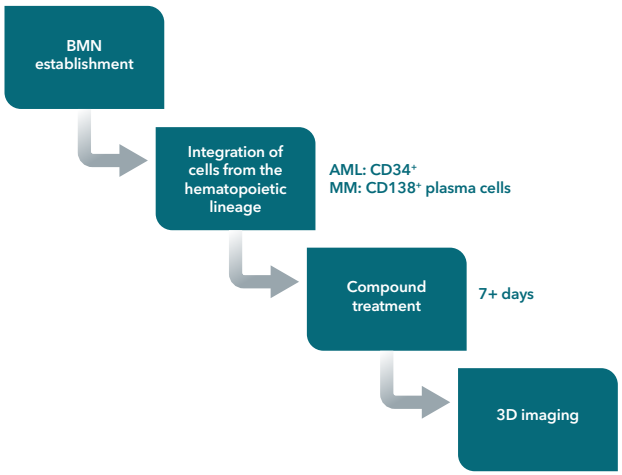
Immune System Integration
Incorporating key immune cell populations to better replicate tumor-immune interactions and enhance translational relevance.

Overview of Bone Marrow Niche Model



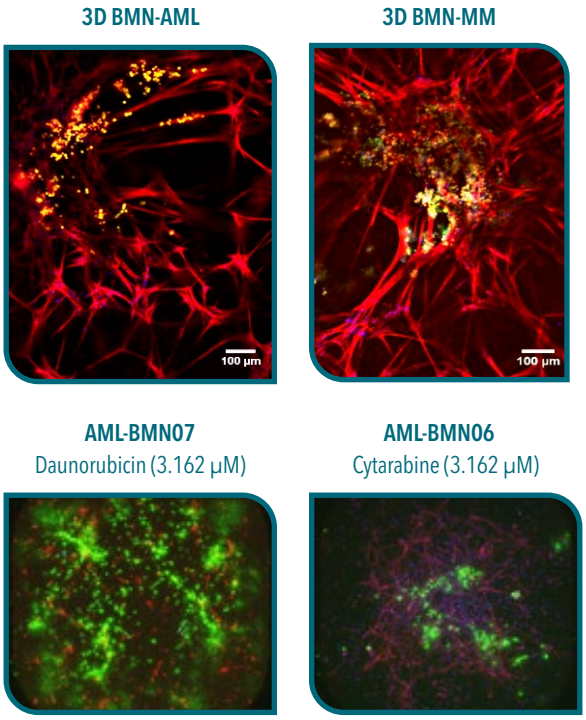
Versatility of the BMN Platform

- A reliable patient-derived hemato-oncology system available for hematological malignancies:
  - Integrate matching patient biospecimens (bone marrow, whole blood, tumor cells and immune cells) to avoid allogeneic responses.
  - Provides endothelial and mesenchymal cell compartments, as well as stiffness to favor vascularization and support for cells of the hematopoietic lineage.
  - Hematopoietic cells can be selected according to the biological question and indication.
  - Patient-specific plate – patient primary cells directly seeded on top of the BMN in a 384-well plate format.
  - Possibility to integrate autologous immune cells.
- Drug effects can be measured by phenotypic high content imaging (HCI) analysis.



Average timeline for a full study: 6-8 weeks upon compound arrival

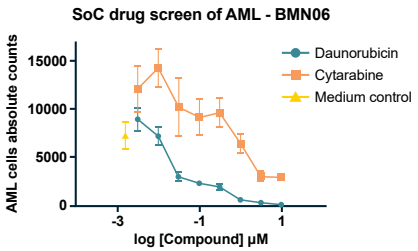
High-content imaging examples of cancer cells adhering to microenvironment

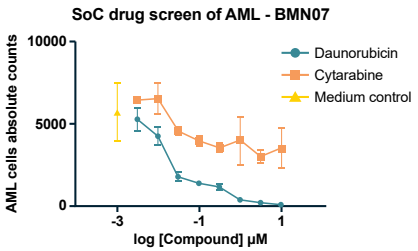


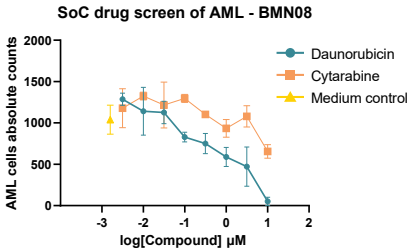
Cell Tracker™ Green | DAPI | Actin

Standard of Care (SoC) drug sensitivity

Patient ID	% Blasts	Immunophenotype	Treatment
AML-BMN06	BM:25% PB:19%	CD45+/-, CD34+/-, CD117+, HLA-DR+, MPO+low, CD14+, CD13+, CD33+	VenAza
AML-BMN07	BM:80% PB:70%	CD45+, CD34+, CD33+, MPO+, CD117+, HLA-DR+, CD13+, CD14+	Naive
AML-BMN08	BM:75% PB:36%	CD45+, MPO+, CD34+, CD117+, HLA DR+, CD13+, CD33+, CD64-, CD38+, CD71+	Naive





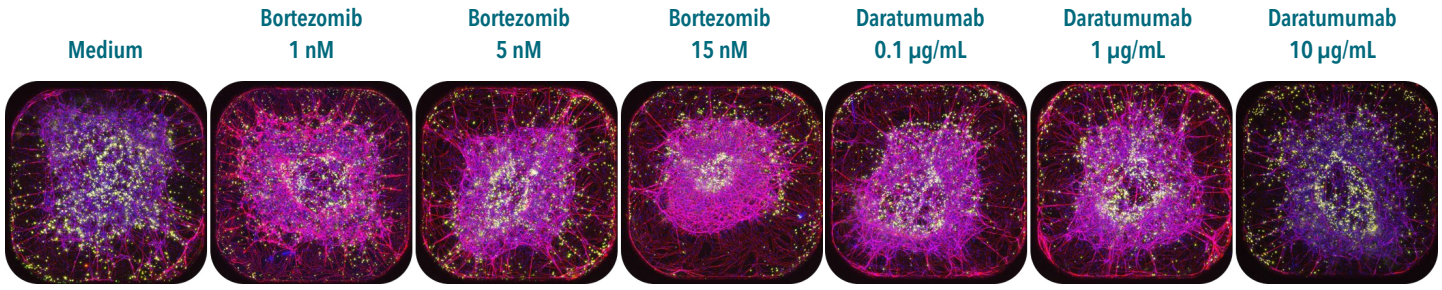


Advance Your Research with Best-in-Class Assays

- **High-Throughput Assays**: Conduct robust assays in a 384-well plate format for maximum efficiency.
- **Diverse Assays Capabilities**: Leverage HCI alongside phenotyping using flow cytometry, immnoflourescence assays, single-cell RNA sequencing, and more.
- **Immune-Competent Assays**: Incorporate immune components to evaluate IO therapies in a relevant microenvironment.
- **Cell Adhesion-Mediated Drug Resistance (CAM-DR) Modeling**: Investigate tumor-microenvironment interactions and their role in therapy resistance to optimize drug efficacy strategies.

3D BMN screening options		Readouts for Hematological Malignancies
Standard	3D BMN drug screening	Assessment of drug sensitivity by HCI
	Baseline immunophenotyping	Flow cytometry analysis
	Patient selection	Detailed patient data and information on previous treatment
Optional	3D BMN off-target screening	Assessment of drug sensitivity by HCI
	3D BMN supernatant	Cytokine analysis from individual replicates
	Target validation	3D Immunofluorescence
	Target validation	RNA-seq analysis

Representative Multiple Myeloma Bone Marrow Niche Models

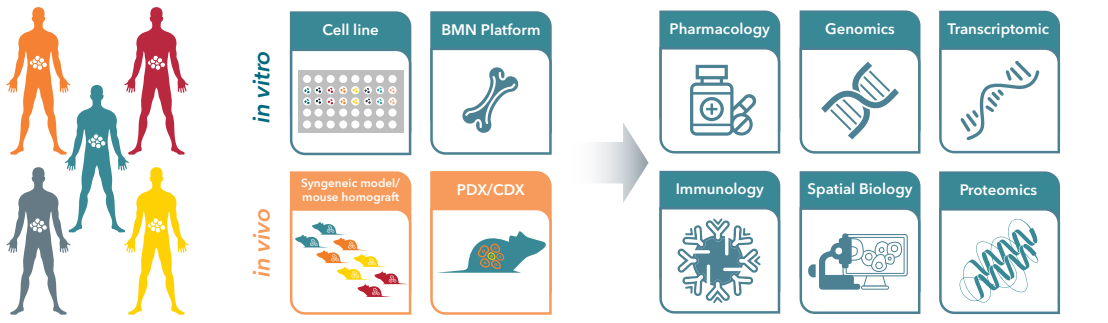


Nuclei | Actin | CD138+

Seamless Transition from *In Vitro* to *In Vivo* to Clinical Trials

We offer a fully integrated platform that enables a smooth progression of research from early discovery to translational studies:

- **Patient-Derived Biobanks** – Well characterized patient tissue containing patient demographics, genomics and treatment history forms the foundation for meaningful studies.
- **3D Bone Marrow Niche Models** – *In vitro* platforms that mimic the native bone marrow environment, preserving tumor viability and allowing for robust drug screening and biomarker discovery.
- **PDX Models** – Patient-derived xenograft (PDX) models provide a predictive *in vivo* system to validate therapeutic efficacy.
- **Comprehensive Biomarker Analysis** – In-depth characterization of drug response and resistance mechanisms through multi-omics and advanced analytics.



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