American Association for Cancer Research

FINDING CURES TOGETHER℠

CICR February 2020 Newsletter

From the Editors, with Dr. Keith Hornberger, Editor-elect

Each quarter, the editorial board selects an area to highlight from the broad range of topics that fall under the umbrella of chemistry in cancer research (CICR). This quarter, we are focusing on targeted protein degradation (TPD). CICR Editorial Board member and editor elect Dr. Keith R. Hornberger has taken the lead in assembling an overview of the topic.

Keith R. Hornberger, PhD

Director, Chemistry, Arvinas, Inc.

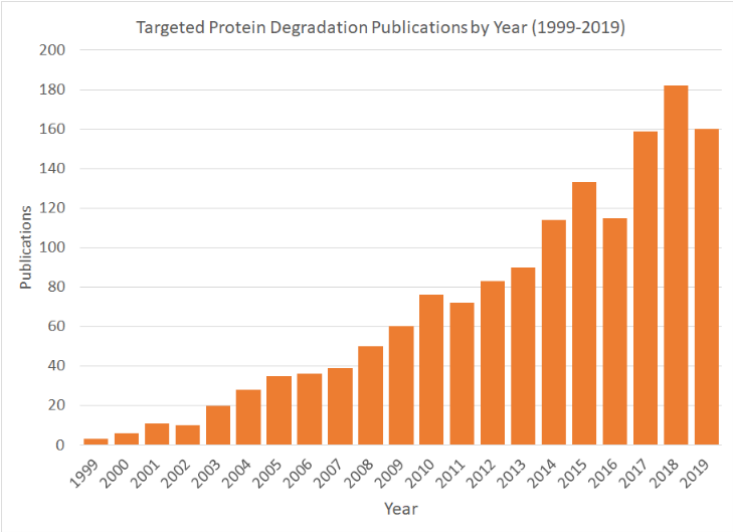
New Haven, CT

Since the first publications nearly 20 years ago, there has been a groundswell of academic and industrial interest in targeted protein degradation (TPD). This trend is reflected in the increased volume of publications around small molecule-induced targeted protein degradation (source: PubMed) and in the increasing number of startup companies founded to pursue TPD therapeutics. 2019 was a watershed year for this new potential therapeutic modality when one of those companies, Arvinas, reported the first-ever clinical trial data for two heterobifunctional protein degraders -- one for the androgen receptor (ARV-110) and another for the estrogen receptor (ARV-471). It is anticipated that more results from the clinical trials of degrader molecules will be reported by others in coming years.

Small molecules causing protein degradation generally fall within two classes, molecular glues and proteolysis targeting chimera (PROTAC® protein degrader) molecules. There are, however, interesting cases where the molecular distinction

between these two classes is blurred and there may be more of a continuum between them.

Pioneered by Celgene and others, molecular glues bind to an E3 ubiquitin ligase and induce the E3 ligase to recruit novel protein substrates ('neosubstrates') to an E3/E2 complex without direct interaction between the glue and the targeted protein substrate. The target protein is then polyubiquitinated by the E3/E2 complex and thus marked for degradation by the proteasome.



The flagship drugs in this class are the immunomodulatory drugs (IMiDs) – thalidomide, lenalidomide, pomalidomide, and others in development. Indeed, lenalidomide (marketed by Celgene as Revlimid®) was the third-best selling drug in the world in 2018, with $9.7 billion in sales. The elucidation of the mechanism of action of these drugs as protein degraders is a fascinating story. Unfortunately for thalidomide, the cause of its teratogenic effects was only explained long after the European thalidomide tragedy of the 1960s.

Reported initially by Crews and Deshaies, proteolysis targeting chimeras – in contrast to molecular glues – are heterobifunctional, containing chemically linked binding moieties to both an E3 ligase and a target protein of interest (POI). These targeted protein degraders directly recruit the POI to an E3/E2 complex, where it is then polyubiquitinated and marked for proteasomal degradation.

The biochemistry of heterobifunctional degraders is complex and leads to phenomena not frequently encountered in small molecule drug discovery. First, the mechanistically productive species is a ternary complex between the POI, the E3, and the degrader molecule. High drug concentrations can lead to saturated binary complexes outcompeting ternary complexes, which results in bell-shaped dose response curves colloquially known as the "hook effect". Ternary complex formation may also result in positive (or negative!) cooperativity of binding via induced interactions between the E3 and POI and/or burying of hydrophobic surface area in the ternary binding interface.
Second, degraders ultimately function through a kinetically irreversible step of protein degradation by the proteasome. A single degrader molecule may cause degradation turnover of multiple POI molecules, resulting in the degrader becoming uncoupled from continuous target occupancy driving efficacy. Targeted protein degraders have been shown in many cases to demonstrate nonlinear pharmacodynamics, with their duration of action exceeding their pharmacokinetics and the rate of protein resynthesis becoming a relevant variable.

Lastly, in a POI-dependent manner, cooperative ternary complex formation and/or degradation turnover efficiency can lead targeted protein degraders to display significant disparities in their binary binding affinities vs. their degradation potency. There are multiple published examples of micromolar binders to either POI or the E3 giving rise to nanomolar degraders, and often with significant changes in target selectivity.

The promise of TPD is substantial. Because targeted protein degraders have a built-in E3 binding handle to supply function, it is not strictly necessary for the POI binder to have a function of its own, but instead only to bind to its target. Degraders also eliminate their target rather than simply occupying a binding site, providing the potential to block protein scaffolding functions, and to have an extended duration of action. These built-in properties may open the door to drugging targets previously considered undruggable or provide therapeutic benefit over traditional inhibitors.

Despite their significant biological potential, heterobifunctional degraders also come with attendant challenges for medicinal chemists. Structure-activity relationships for degradation may be nonlinear due to their complex biochemistry. Further, owing to their size and physicochemical properties, such molecules are squarely in what Kihlberg characterized as “beyond Rule of 5” (bRo5) property space. Consistently attaining oral bioavailability with such molecules remains an ongoing design challenge and area of active investigation.

In this issue, the editorial board has collected a series of research highlights that speak to both the promise and the challenges of this new therapeutic modality.

Some review articles that serve as a jumping-off point for further reading:

1. Chamberlain, PP; Hamann, LG, *Nature Chem Biol* 2019;15:937-944
2. Pettersson, M; Crews, CM, *Drug Disc Today Tech* 2019;31:15-27
3. Paiva, S-L; Crews, CM, *Curr Opin Chem Biol* 2019;50:111-119
4. Fisher, SL; Phillips, AJ, *Curr Opin Chem Biol* 2018;44:47-55
5. Zhang, Y et al, *Drug Disc Today Tech* 2019;31:53-60

Join the new AACR-CICR LinkedIn Network Group

We look forward to your participation in our conversations that are designed to enhance your CICR initiative. Join the group.

View the CICR Newsletter Archives & the CICR Early-career Researcher Profiles Archives

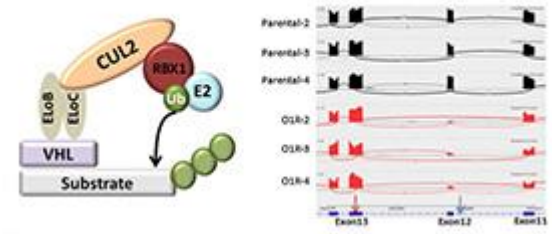
For past issues of the CICR Newsletter, visit its Archives. We are also pleased to provide past issues' Profiles of Early-career Researchers in its own Archives.

Molecular Cancer Therapeutics Highlight

We highlight a recent article from Molecular Cancer Therapeutics in every Newsletter. This quarter’s highlight is related to the issue’s topic on targeted protein degradation. The article is also included in the Research Highlights section.

Acquired resistance to BET-PROTACs (proteolysis-targeting chimeras) caused by genomic alterations in core components of E3 ligase complexes
Zhang, L et al, *Mol Cancer Ther*, 2019;18:1302-11

Acquired resistance: PROTACs are bifunctional molecules that hijack endogenous E3 ubiquitin ligases to induce degradation of protein of interest. With PROTAC technology progressing rapidly towards therapeutic applications, it would be important to understand whether and how resistance to these novel agents may emerge. Using BET-PROTACs as a model system, Zhang and colleagues demonstrate that resistance to both VHL- and CRBN-based PROTACs was primarily caused by genomic alterations that compromise core components of the relevant E3 ligase complexes. This study reveals a novel resistance mechanism distinct from current targeted therapies and lay the foundation for future investigations.



News from the CICR Steering Committee

CICR Newsletter for February 2020
Dr. Andrew J. Phillips, CICR Chairperson 2019-2020

JOIN US AT THE AACR ANNUAL MEETING 2020!

On behalf of all CICR Steering Committee members, Happy 2020! We look forward to seeing all CICR members and colleagues at the AACR Annual Meeting 2020 in San Diego, California (April 24-29, 2020), particularly at the CICR sessions and events! A CICR Town Hall will be held on Sunday, April 26, 5:30-7 p.m., San Diego Convention Center, room to be announced, immediately following the two always-popular CICR-sponsored *New Drugs on the Horizon sessions* (the inaugural third-part of this session will be held on April 27, 10:30 a.m.-12:30 p.m.) which will comprise exciting presentations on first disclosures of new anticancer agents in or soon to be in clinical trials. This is an excellent opportunity to learn about the next wave of innovative cancer drugs progressing in the clinic. In addition, the CICR Steering Committee has organized a stimulating three-part *Chemistry to the Clinic* educational session being held on Saturday, April 25, 2020, beginning at 8 a.m. in the Convention Center. These three sessions are programmed to provide informative content to benefit cancer chemistry research, and are listed as follows:

- Lead Optimization Case Studies in Cancer Drug Discovery, chaired by Michael Brands and Joachim Rudolph
- Irreversible Inhibitors as Potential Anticancer Agents, chaired by Sara J. Buhrlage and Richard A. Ward
- Next-Generation Medicines on Clinically Useful Targets, chaired by Xiaojing (Gina) Wang and Stephen E. Fawell

Please encourage your colleagues to attend these sessions at the Annual Meeting 2020, since a major turnout will support the efforts of the CICR Working Group to organize such stimulating sessions and emphasize the crucial role that chemistry plays in cancer research.

JOIN THE AACR-CICR LINKEDIN NETWORK GROUP!

If you haven't done so already, make sure to join this exciting LinkedIn Group that focuses on "all things CICR!" We look forward to your active participation to ensure stimulating conversations as well as research and programming updates.

CONTACT US

Thank you for your continued support! For questions or comments, please email cicr@aacr.org. We are happy to hear from you!

Selected Research Highlights

Many facets of BTK degradation: BTK has been of considerable literature interest as a target for degradation. The FDA-approved BTK inhibitors are all irreversible covalent modifiers of an active site cysteine and are thus subject to resistance via mutation of this cysteine. In this set of manuscripts, BTK degradation is examined by several different approaches:

1. The Crews lab prepare degraders by modifications to ibrutinib that overcome the clinically relevant C481S resistance mutation.
2. Researchers at Pfizer showcase robust degradation of BTK driven by catalytic turnover rather than ternary complex cooperativity.
3. Tinworth *et al*. demonstrate that BTK degraders based on an irreversible warhead are limited in utility due to their inability to undergo catalytic turnover.
4. Guo *et al*. show that reversible covalent modifications of the extant BTK warheads can overcome this limitation to provide very robust target degradation.

Targeting the C481S Ibrutinib-resistance mutation in Bruton's Tyrosine Kinase using PROTAC-mediated degradation. Buhimschi, AD et al. *Biochemistry* 2018;57:3564-3575

Delineating the role of cooperativity in the design of potent PROTACs for BTK. Zorba, A et al. *Proc Natl Acad Sci USA* 2018;115:E7285-E7292

PROTAC-mediated degradation of Bruton's Tyrosine Kinase is inhibited by covalent binding. Tinworth, CP et al. *ACS Chem Biol* 2019;14:342-347

Enhancing intracellular concentration and target engagement of PROTACs with reversible covalent chemistry. Guo, W-H et al. bioRxiv 2019;12.30.873588

Surprising selectivity: Many examples have been reported describing how targeted protein degraders can achieve a surprising degree of target specificity/selectivity, which in many cases appears driven by differential ternary complex formation -- even when the moiety targeting the protein of interest binds to highly homologous active sites. Highlighted examples are:

1. Selective degradation of p38 alpha or delta isoforms simply by changing the spatial presentation of the same E3 ligase.
2. Selective degradation of CDK4/CDK6 starting from a nonselective warhead, palbociclib.
3. Selective degradation of Mcl-1 or Bcl-2, also starting from a nonselective warhead.

Differential PROTAC substrate specificity dictated by orientation of recruited E3 ligase. Smith, BE et al. *Nature Commun* 2019;10,131

Selective degradation of CDK6 by a palbociclib based PROTAC. Rana, S et al. *Bioorg Med Chem Lett* 2019;29:1375-1379

Development of dual and selective degraders of cyclin-dependent kinases 4 and 6. Jiang, B et al. *Angew Chem Int Ed* 2019;58:6321-6326

Proteolysis targeting chimeras for the selective degradation of Mcl-1/Bcl-2 derived from nonselective target binding ligands. Wang, Z et al. *J Med Chem* 2019;62:8152-8163

Macrocyclic PROTACs based on MZ1: The structure-based analysis of the MZ1:Brd4:VHL complex guided the design and synthesis of a macrocylic PROTACs that features better discrimination between closely related BET domains in biochemical assays and comparable activity in cells.

Structure - based design of a macrocyclic PROTAC. Testa, A et al. Angew Chem Int Ed 2020;58:2-10

Drugging the undruggable: Two recent reports highlight the opportunities and the challenges for use of targeted protein degradation to access classically undruggable targets. In the first, the Wang group report the highly selective and prolonged degradation of the transcription factor STAT3, which is mutated or dysregulated in many cancers. In the second, the Gray group report progress toward degraders of $KRAS^{G12C}$ using irreversible covalent modifiers as warheads. Such degraders were capable of degrading GFP tagged $KRAS^{G12C}$ but not the native protein, suggesting in some cases that degraders may continue to face challenges as inhibitors do with undruggable targets. This example also reinforces the importance of careful assessment of the tagging strategy used for reading out degradation in cell-based assays.

Structure-based discovery of SD-36 as a potent, selective, and efficacious PROTAC degrader of STAT3 protein. Zhou, H et al. *J Med Chem* 2019;62:11280-11300

Exploring targeted degradation strategy for oncogenic KRAS G12C. Zeng, M et al. *Cell Chem Biol* 2020;27:1-13

Oral drug design challenges: Targeted protein degraders are large, heterobifunctional molecules, and as such generally lie in the “Beyond Rule of 5” (bRo5) property space where the probability of oral absorption is diminished. The reviews from Edmondson *et a*l. and Maple *et al.* summarize the extant literature on the physicochemical property space and oral bioavailability potential of degrader molecules and highlight paths forward. The manuscript from the Frye group at UNC highlights the use of a novel method to estimate the permeability of degrader molecules, which often perform poorly in traditional ADME assays used to measure permeability.

Proteolysis targeting chimeras (PROTACs) in ‘beyond rule-of-five’ chemical space: Recent progress and future challenges. Edmondson, SD et al. *Bioorg Med Chem Lett* 2019;29:1555-1564

Developing degraders: principles and perspectives on design and chemical space. Maple, HJ et al. *MedChemComm* 2019;10:1755-1764

Assessing the cell permeability of bivalent chemical degraders using the chloroalkane penetration assay. Foley, CA et al. *ACS Chem Biol* 2020;15:290-295

Assessing PROTAC cellular penetration: Bivalent PROTACs molecules push the boundary of "small" molecules, with notable effects on permeability and other properties. The authors of this paper generate "structure-permeability" relationships using a Halotag-like cellular penetration assay, with results that are different than those obtained with a more standard Caco-2 assay.

Assessing the cell permeability of bivalent chemical degraders using the chloroalkane penetration assay. Foley, CA et al. *ACS Chem Biol* 2020;15:290-295

All it takes is micromolar: Using a weaker VHL ligand conjugated to an AR ligand, the authors demonstrate that effective protein degradation can be obtained even from a bivalent molecule that binds to an E3 ligase complex with only low micromolar affinity.

Discovery of highly potent and efficient PROTAC degraders of androgen receptor (AR) by employing weak binding affinity VHL E3 ligase ligands. Han X et al, *J Med Chem* 2019;62:11218-11231

Acquired resistance: PROTACs are bifunctional molecules that hijack endogenous E3 ubiquitin ligases to induce degradation of protein of interest. With PROTAC technology progressing rapidly towards therapeutic applications, it would be important to understand whether and how resistance to these novel agents may emerge. Using BET-PROTACs as a model system, Zhang and colleagues demonstrate that resistance to both VHL- and CRBN-based PROTACs was primarily caused by genomic alterations that compromise core components of the relevant E3 ligase complexes. This study reveals a novel resistance mechanism distinct from current targeted therapies and lay the foundation for future investigations.

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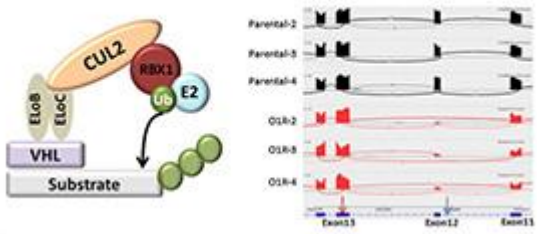


Lipophilic contributions of common functional groups: Genentech scientists leveraged their internal LogD data collection (pH 7.4), experimentally derived from a large and pharmaceutically relevant set of compounds, to define a list of experimentally

determined delta-logD values for common molecular fragments. The list provides a generalized sense for the lipophilic contributions of commonly employed substituents in the context of drug-like molecules.

LogD contributions of substituents commonly used in medicinal chemistry. Landry, ML; Crawford, JJ, *ACS Med Chem Lett* 2020;11:72-76

Profile of an Early-Career Researcher

Dr. Erika M. Vieira Araujo

Research Investigator

Arvinas, Inc.

New Haven, CT

This issue's Early Career Profile highlights Dr. Erika Vieira Araujo who is currently a Research Investigator at Arvinas, a biotechnology company solely focused on bringing PROTAC® molecules (heterobifunctional protein degraders) to the clinic. As a medicinal chemist, Erika co-leads several projects at Arvinas aimed at using targeted protein degradation to treat cancer. Within this role she has learned how to use her knowledge of medicinal chemistry to design tripartite "beyond Rule of 5" molecules, consisting of a ligand to a targeted protein, a linker, and a ligand capable of recruiting an E3 ligase. Alongside her colleagues at Arvinas, Erika is working to understand the unique and fascinating biology, pharmacology and physicochemical properties presented by this therapeutic modality.

Erika Araujo earned her Ph.D. in organic chemistry under the supervision of Professor Amir Hoveyda in 2013. During her doctoral studies, she discovered novel methods and catalysts for the enantioselective preparation of amines and alcohols. Her research at Boston College was recognized with several awards including an AstraZeneca Fellowship, an Eli Lilly Travel Grant, an Abbott Scholar Award, and several invited presentations. Prior to her graduate studies, Erika obtained her Bachelor of Science degree in chemistry in 2006 from Fairfield University where she was introduced to research by Professor Joseph Sarneski.

Following completion of her Ph.D., Erika joined Bristol-Myers Squibb in the Discovery Chemistry group in Wallingford, Connecticut. She worked on both hit-to-lead and lead optimization programs for the identification of selective kinase inhibitors for oncology and immuno-oncology indications. Her time at Bristol-Myers Squibb rooted a passion for medicinal chemistry and oncology which ultimately led to her current position tackling malignant proteins with chemically induced proteasomal degradation.

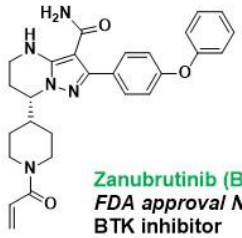
Erika has been a coauthor on nine publications and patents and was an invited speaker to present on PROTAC® degraders at the Fall 2019 ACS MEDI Rising Stars: Women in Medicinal Chemistry Symposium. She also volunteers her time to serve on the ACS Division of Medicinal Chemistry Executive Committee as a Member-at-Large since 2017 as well as chairing the Young Medicinal Chemists Committee for MEDI. In her role with MEDI, she is focused on energizing and attracting the younger generation of drug discoverers to become engaged members of MEDI. She is also a proponent for the use of social media for science communication and outreach.

Global News

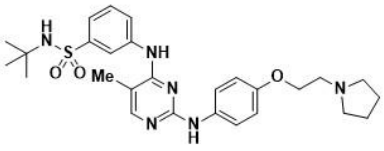
Note: Discussion of FDA approvals for this issue are limited to new chemical entities approved to treat cancer since the previous issue Oct 2019.

A "friendly" FDA in 2019: The FDA approved 45 new drugs in 2019, reflecting a general uptick in approvals since 2016. Cancer leads all indications, with 11 new approvals. Source: FierceBiotech, C&ENews

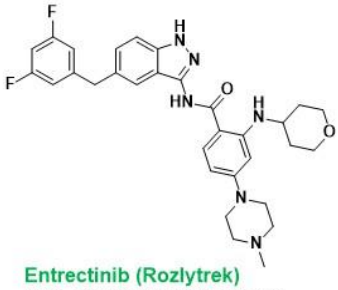
2019 FDA Approvals (Oncology) - Small Molecule NMEs



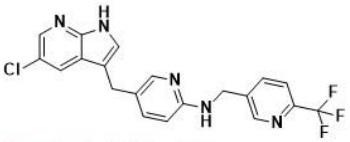
Zanubrutinib (Brukinsa)
FDA approval Nov 14, 2019
BTK inhibitor
Mantle cell lymphoma



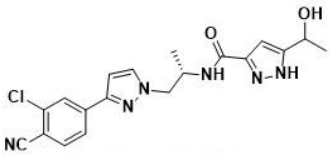
Fedratinib (Inrebic)
FDA approval Aug 16, 2019
JAK2/FLT3 inhibitor
Myelofibrosis



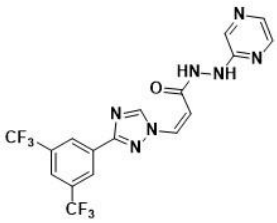
Entrectinib (Rozlytrek)
FDA approval Aug 15, 2019
pan-Trk/ROS1/Alk inhibitor
ROS1-positive NSCLC



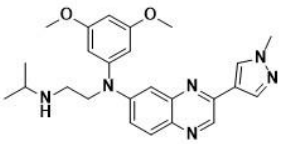
Pexidartinib (Turalio)
FDA approval Aug 2, 2019
CSF1R/KIT/FLT3 inhibitor
Tenosynovial giant cell tumour



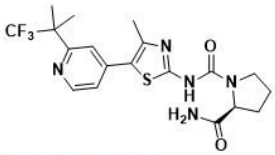
Darolutamide (Nubeqa)
FDA approval July 30, 2019
androgen receptor antagonist
Prostate cancer



Selinexor (Xpovio)
FDA approval July 3, 2019
CRM1/XPO1 antagonist
Multiple myeloma



Erdafitinib (Balversa)
FDA approval April 12, 2019
pan-FGFR inhibitor
Bladder cancer

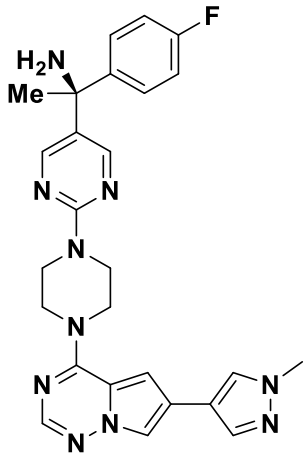


Alpelisib (Piqray)
FDA approval May 24, 2019
PI3Kα inhibitor
Breast cancer

Merck buys ArQule: Keyed by the successes with ARQ 531, a BTK inhibitor in Phase II, Merck has acquired ArQule for $ 2.7 billion to strengthen its oncology pipeline. Source: Merck

E3 ligase companies proliferate: Emerging biotech company Plexium is using a proprietary DEL screening platform to take on E3 ligases, joining companies such as Arvinas, Kymera, C4, Cedilla, and Nurix in using these proteins to discover new therapies by manipulating protein degradation. Source: BusinessWire

FDA approval of avapritinib (Ayvakit): On January 9, 2020 Blueprint received the first FDA approval of the New Year, for the kinase inhibitor avapritinib (Ayvakit), to treat adults with unresectable or metastatic gastrointestinal stromal tumor (GIST). The compound is an inhibitor of platelet-derived growth factor receptor alpha (PDGFRA) and targets the PDGFRA exon 18 mutation, but also inhibits c-KIT kinase. The approval marks the first approval for Blueprint Medicines and provides an effective targeted therapy towards a subset of GIST patients who do not respond to the current standard of care. Sources: FDA, BioPharmaDive, FiercePharma

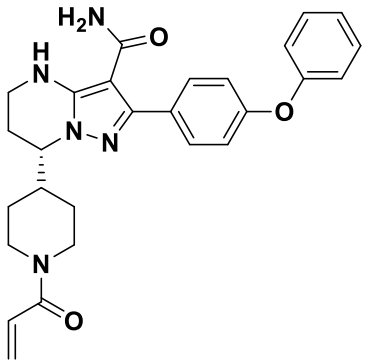


FDA approval of trastuzumab deruxtecan (Enhertu): On Dec 20, 2019 Daiichi Sankyo received approval for the antibody drug conjugate fam-trastuzumab deruxtecan-nxki (Enhertu) for the treatment of metastatic breast cancer. This ADC consists of the approved HER2-directed antibody trastuzumab appended to the cytotoxic topoisomerase I inhibitor deruxtecan. ADCs are a therapeutic modality that has exploded in recent years with many new approvals and advances and the topic has recently been highlighted in the May 2019 CICR Newsletter. See related blogpost. Source: FDA

FDA approval of enfortumab vedotin (Padcev): On Dec 18, 2019 Astellas Pharma received approval for the antibody drug conjugate (ADC) enfortumab vedotin-ejfv (Padcev) to treat refractory bladder cancer. ADCs are a therapeutic modality that has exploded in recent years with many new approvals and advances and the topic has recently been highlighted in the May 2019 CICR Newsletter. This antibody-drug conjugate comprises the antimitotic drug monomethyl auristatin E (MMAE, vedotin) attached to the monoclonal antibody enfortumab. Source: FDA

FDA approval of zanubrutinib (Brukinsa): The BTK inhibitor zanubrutinib (Brukinsa, BeiGene) was approved on Nov 14, 2019 to treat certain patients with mantle cell lymphoma (MCL), a form of blood cancer. This is the third approval of a BTK inhibitor following ibrutinib (Pharmacyclics/Johnson & Johnson, 2013) and acalabrutinib (Acerta Pharma/Astra Zeneca, 2017). Like other approved BTK inhibitors, the

molecule is an irreversible drug which contains a Michael acceptor as the covalent warhead. Source: FDA



Upcoming Conferences and Events

To aid those who are contemplating attending a conference we compile a list of upcoming meetings that might interest a scientist in the field of chemistry in cancer research. For an extensive calendar of AACR related meetings please check the searchable AACR Meetings and Workshops Calendar on the AACR website.

Frontiers in Medicinal Chemistry
March 22-25, 2020; Freiburg, Germany

259th ACS National Meeting and Expo
March 22-26, 2020; Philadelphia, Pennsylvania

15th CHI Fragment-Based Drug Discovery
April 13-17, 2020; San Diego, California

AACR Annual Meeting 2020
April 24-29, 2020; San Diego, California

102nd Canadian Chemistry Conference and Exhibition
May 24-28, 2020; Winnipeg, Manitoba, Canada

Kinase 2020: 9th RSC/SCI Symposium on Kinase Inhibitor Design
June 1-2, 2020; London, United Kingdom

8th NovAliX Conference
June 15-17, 2020; Boston, Massachusetts

Gordon Research Conference in Heterocyclic Compounds 2020
June 21-26, 2020; Newport, Rhode Island

ACS MEDI 37th National Medicinal Chemistry Symposium
June 28 - July 1, 2020; New York, New York

RICT 2020, 56th International Conference on Medicinal Chemistry
July 1-3, 2020; Bordeaux, France

Gordon Research Conference in Organic Reactions & Processes 2020
July 19-24, 2020; Smithfield, Rhode Island

Gordon Research Conference in Natural Products & Bioactive Compounds 2020
August 2-7, 2020; Andover, New Hampshire

Gordon Research Conference in Medicinal Chemistry 2020
August 9-14, 2020; New London, New Hampshire

260th ACS National Meeting & Exposition
August 23-27, 2020; San Francisco, California

Fragment-Based Lead Discovery 2020
Sept. 20-23, 2020; Cambridge, United Kingdom

Funding Opportunities

Please check the searchable AACR Funding Opportunities page for a current listing of available AACR grant opportunities.

- OPEN AACR-AstraZeneca Stimulating Therapeutic Advances through Research Training (START) Grants

  Grant Amount: *$225,000 USD* **Application Deadline:** *1/22/2020* **Decision Date:** *3/2020* **Start of Grant Term:** 7/1/2020

  Grant Duration: 3 years

- OPEN AACR-Triple Negative Breast Cancer Foundation Research Fellowship

  Grant Amount: *$180,000 USD* **Application Deadline:** *1/28/2020* **Decision Date:** *3/2020* **Start of Grant Term:** 7/1/2020

  Grant Duration: 3 years

- OPEN AACR Lung Cancer Research Fellowships

  Grant Amount: *$120,000 USD* **Application Deadline:** *1/28/2020* **Decision Date:** *3/2020* **Start of Grant Term:** 7/1/2020

  Grant Duration: 2 years

- OPEN AACR-PLGA Fund at the Pediatric Brain Tumor Foundation Research Grant to Optimize Drug Dosing Strategies for Pediatric LGA/LGG Patients

  Grant Amount: *$180,000 USD* **Application Deadline:** *2/18/2020* **Decision Date:** *3/2020* **Start of Grant Term:** 7/1/2020

  Grant Duration: 2 years

- OPEN AACR-Bayer Innovation and Discovery Grants

  Grant Amount: *$50,000 USD* **Application Deadline:** *2/25/2020* **Decision Date:** *3/2020* **Start of Grant Term:** 7/1/2020

  Grant Duration: 1 years

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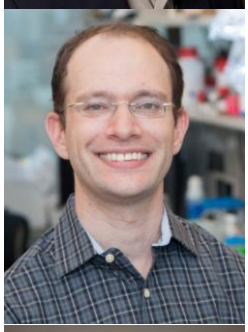

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