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The San Diego Chemist

San Diego Section

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ACS/SABPA
Chemistry Symposium

PROCESS CHEMISTRY IN THE DEVELOPMENT OF KRAS DRUGS



**Tuesday, November 7,
2023**



4:00 PM - 8:00 PM



**Novartis
10675 John Jay Hopkins Dr,
San Diego, CA 92121**



SPEAKER

Dr. Xiaohu Deng

Former Head of CMC
at Wellspring Biosciences



SPEAKER

Dr. Cheng Yi Chen

VP of Chemistry
Process R&D at Mirati



SPEAKER

Dr. Haiming Zhang

Distinguished Scientist and
Director at Genentech

Upcoming event!

**End-of-year Meeting
and Holiday Party
December 7, 2023
6:30PM
The Butcher Shop
Steakhouse
[Register here!](#)**

Dear esteemed members,

This year's National Chemistry Week theme was the Healing Power of Chemistry. The San Diego Local Section likely exemplifies this theme better than any other Local Section. This month, we feature a flagship event you will not want to miss. Join us for **Process Chemistry in the Development of KRAS Drugs on Tuesday, November 7th** at 4 PM at the **Novartis Research Foundation**. We will feature three distinguished leaders in the bio-pharmaceutical space working on developing and scaling up novel and promising therapies for cancer patients. **Dr. Xiaohu Deng**, Former Head of CMC at Wellspring Biosciences will deliver a presentation called, "Scaleup Efforts on the Production of the First-generation, Atropisomeric Covalent KRAS G12C Inhibitors ARS-1620 and ARS-2102." He will be followed by **Dr. Cheng Yi Chen**, Vice President of Chemistry Process R&D at Mirati. For his talk, Dr. Chen will present "Adagrasib (MRTX849) Commercial Route." The seminar will conclude with "Development of an Atroposelective Process of KRAS G12C Inhibitor GDC-6036" by **Dr. Haiming Zhang**, Director at Genentech. This event is free and starts with a networking hour; refreshments will be provided. [Register here!](#)

In October, we brought you two excellent seminars showcasing the inspirational ability of chemistry to improve the quality of life for humanity. Thank you to Ms. **Nga Do** for giving us a glimpse into the mammoth behind-the-scenes work that she and her colleagues at Pfizer undertook to bring **Nirmatrelvir** to market in a blistering 17 months! This seminar, as well as this month's flagship event, is a **collaboration between the San Diego Local Section and the SoCal Association for Biomedical and Pharmaceutical Advancements (SABPA)**. I look forward to working with our SABPA colleagues to bring you more exciting medicinal chemistry-themed events. I also thank **Dr. H.N Cheng** for his engaging and informative presentation on plastic pollution and the current state of developments in the search for biodegradable plastic candidates, which may one day hopefully replace disposable, petroleum-based plastic. [Click here](#) to (re)watch Dr. Cheng's presentation.

Chem Expo was also a big hit this year. Over 200 members of the public and science enthusiasts descending on Miramar College to learn about the healing power of chemistry, engage in educational hands-on projects, and watch fun demos conducted by our Local Section Student Affiliate Chapters. The **University of San Diego, CSU San Marcos, UC San Diego, Point Loma Nazarene University, Mesa College**, and my (awesome) **Southwestern College** students all did a fantastic job and had lots of fun doing it.

Also, this month is the Local Section elections, so **do not forget to vote!** You will receive an electronic ballot at the email address the national ACS has on file for you. As long as you are a dues-paying member, you are eligible to cast a vote for your Local Section leadership. Be on the lookout for your ballot around the 15th of the month. If you have any questions or concerns about your ballot, reach out to my colleague, **Jackie Trischman** (trischma@csusm.edu), who serves as the Local Section election coordinator.

Lastly, celebrate our last hurrah of 2023 at the **End-of-Year Meeting and Holiday Party at the Butcher Shop Steakhouse** on **December 7th at 6:30 PM**. Expect a delectable buffet-style dinner and excellent camaraderie. There, we will announce the results of the upcoming election; I will give my farewell address, and introduce my successor. [Click here to register](#).

On that note, I will close by expressing that I am thankful for all of you, the members, who do your part to advance our discipline and make our chemically-minded community the best one in the world. I wish you and your loved ones a beautiful Thanksgiving.

With gratitude,

Juan Gonzalez

2023 Chair, San Diego Section of the American Chemical Society

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Web: www.sandiegoacs.org

Scaleup Efforts on the Production of the First-generation, Atropisomeric Covalent KRAS G12C Inhibitors ARS-1620 and ARS-2102

Dr. Xiaohu Deng,

**Former Head of CMC
at Wellspring Biosciences**



About the Speaker

Dr. Deng is a seasoned executive with >22 years of experience in the pharmaceutical and biotechnology industry with the focus on drug product development and technical operations. He was a Sr. Vice President, Head of Technical Operations at Vividion Therapeutics from 2021 to 2023, leading the department encompassing preclinical formulation, API process development, drug product formulation development, DS and DP cGMP manufacturing, analytical development, quality control and clinical supply. Prior to Vividion, he served as a Senior Vice President, Product Development at Viracta Therapeutics, leading the CMC function and IP strategy. Prior to that, he was a Senior Director, Head of CMC at Kura Oncology and Wellspring Biosciences, overseeing the CMC efforts on process R&D, manufacturing, compliance, regulatory and clinical supply for multiple programs from preclinical to registrational phases. Dr. Deng started his industry career at Janssen Pharmaceutical Companies of Johnson & Johnson, involved in process R&D, CRO management and project management on drug discovery and preclinical development.

Dr. Deng holds a Ph.D. in organic chemistry from Emory University, and an M.S. in physical chemistry and a B.S. in chemistry from Fudan University. Dr. Deng has more than 40 journal publications, a book chapter and 18 published patents to his credit.

About the Talk

ARS-1620 is the first reported KRAS G12C inhibitor that showed single agent antitumor activities in multiple human cancer cell line- and patient-derived mouse xenograft tumor models. It is potent, selective, orally bioavailable, and well-tolerated in mice. A synthetic strategy that relies on metalation of substituted quinazolines at C7 was designed to achieve the exquisite selectivity to enable the scalable routes to kilogram production of ARS-1620 and related analogs in this family.

A follow-on drug candidate, ARS-2102 was advanced for the preclinical development. An “early cross-coupling” strategy was utilized to construct the tetra-substituted atropisomeric biaryl core. An iterative diastereomeric recrystallization enabled an effective chiral resolution of key intermediate. A global deprotection followed by chemoselective functionalization afforded ARS-2102 in excellent yield and diastereomeric enrichment. This chromatography-free sequence was successfully executed on kilogram scale.

Adagrasib (MRTX849) Commercial Route

Dr. Cheng Yi Chen

**VP of Chemistry Process
R&D at Mirati**



About the Speaker

Cheng received his BS in Chemistry at Xiamen University in 1984 and subsequently continued his PhD study at the Ohio State University from 1985-1990. He singlehandedly completed the first total synthesis of the stemona alkaloid, stenine. He then joined the Process Chemistry department at Merck Research Laboratories in Rahway, NJ and worked there till the end of 2013. In 2014, he joined Janssen Pharmaceuticals of JNJ in Switzerland as a scientific advisor. In 2019, Cheng returned to San Diego and joined Mirati Therapeutics as the head of Chemical Processing R&D. He is currently leading a group of 10 process chemists and is responsible for all the activities related to the drug substances. Cheng has more than 100 publications and patents.

About the Talk

Adagrasib (MRTX849), a Kras G12C inhibitor sold under the brand name Krazati, is an anticancer medication used to treat non-small cell lung cancer. A commercial route to adagrasib was developed to support clinical and commercial needs. Yield was improved to 32% over six chemical steps. Recently, a new, five-step, chromatography-free synthesis of adagrasib from readily available starting materials was developed which obviated the palladium catalysis and protecting group manipulations in the current commercial route and significantly improved the efficiency of the process in 45% overall yield. The chemical development of both routes will be presented.

Development of an Atroposelective Process of KRAS G12C Inhibitor GDC-6036

Dr. Haiming Zhang

**Distinguished Scientist and
Director at Genentech**



About the Speaker

Haiming obtained both his B.S. and M.S. degrees from the University of Science and Technology of China and his Ph.D. from Iowa State University under the direction of Prof. Richard Larock. He then did two years of postdoc with Prof. Brian Stoltz at Caltech working on CH Functionalization chemistry and total synthesis of natural product telomestatin. Haiming started his industrial career at Lexicon Pharmaceuticals in Princeton NJ in 2005 and moved to Genentech in 2010. He is currently a Distinguished Scientist and Director in the Small Molecule Process Chemistry department at Genentech. Haiming was the recipient of ACS DOC's Young Investigator Award in 2016 and Mid-Career Award in 2022. He is a coauthor or co-inventor of more than 100 publications and patents

About the Talk

The evolution of our process development of an atroposelective synthesis of KRAS G12C Inhibitor GDC-6036 is described. The selected process incorporates a key intermediate synthesis by a practical atroposelective cross-coupling which allows the manufacture of the Active Pharmaceutical Ingredient (API) GDC-6036 at >100 kg scale to support our fast-moving clinical development.



2023

*Distinguished
Scientist*





YOU ARE INVITED TO OUR



End-of-Year Meeting and Holiday Party



DECEMBER 7, 2023
6:30PM
THE BUTCHER SHOP STEAKHOUSE



REGISTER NOW!

Tuesday, November 7, 2023

ACS/SABPA Seminar

***Topic:* CMC/process development of each company's
KRAS G12C inhibitors**

Speakers:

**Dr. Chengyi Chen,
VP of Chemistry Process R&D at Mirati Adagrasib (MRTX849)**

**Dr. Xiaohu Deng,
Former Head of CMC at Wellspring Biosciences**

**Dr. Haiming Zhang,
Distinguished Scientist and Director at Genentech**

***Location:* Novartis**

***Time:* 4PM - 8PM**

[Register here!](#)

End-of-year Meeting and Holiday Party

December 7, 2023

6:30PM

The Butcher Shop Steakhouse

[Register here!](#)

How to Optimize Formulation &
Measurement with a Unified Laboratory
Informatics Solution
November 9, 2023
8:00 AM PST
[Click here!](#)



Biophysical and Structural Biology
Methods Enable Fragment-Based Ligand
Discovery
November 15, 2023
8:00 a.m. PST
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Unbreakable Design: The Polymer
Mechanochemistry of Self-Healing Materials
ACS Webinars
November 16, 2023
11:00 AM PST
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Medicamentos en el Medio Ambiente: Desafíos
y Soluciones a través de la Ecofarmacovigilancia
ACS Webinars
November 22, 2023
[Click here!](#)

No Compromises, Native Molecule Drug
Discovery Assays Using Mass Spectrometry
November 30, 2023
8:00 a.m. PST
[Click here!](#)

**San Diego Section, American Chemical Society
Executive Committee – Zoom Meeting
Nov. 2, 2023, 6:30 p.m.**

Attendees: Sean Anderson, Surya De, Juan Gonzalez-Gonzalez (chair), Carolina Ibarra, Valerie Kuck, Julann Miller, Jim O'Brien, Jim Shih, Mark Tichenor, Bill Tolley, (secretary), Jackie Trischman, Christina Vialva, David Wallace

Visitors: Alessandro Fracassi, Stayam

September & October ExComm Minutes (JGG) – Approved (typo in Oct. treasurer's report)

Treasurer's Report (JGG for DG) – Income: sponsorships: \$1000 WuXi AppTec, \$600 TargetMol (for Distinguished Scientist dinner), \$1278.53 from Eventbrite for Distinguished Scientist dinner admission; ~\$62 from SDCCU interest; expenses: \$900 for ChemExpo permit from Miramar College, \$5,798.08 for Distinguished Scientist Award dinner (total expense of \$6,298.08 including the \$500 deposit), \$49.98 – Eventbrite fee for monthly meetings (2 invoices for \$24.99 each), \$45.54 for some additional picnic stuff, \$155 for storage unit, \$1500 to awardees, and \$127.82 for plaque engraving for Distinguished Scientist program, \$125 for 3 electronic cables, \$450 for October Newsletter preparation, \$444 for social media activities, \$300 for last 6 months of Web hosting and maintenance; Financial assets \$13K over last year

October Seminars (DW) – October 24, 2023 -- Nirmatrelvir development story, co-organizers ACS/SABPA, speaker: Ms. Nga Do, Principal Scientist at Pfizer (Groton, Connecticut), large number of registrants, ~75 attending, a good number of new attendees; October 26, 2023 -- Tackling the Plastic Pollution Problem, speaker: H. N. Cheng (Past President, American Chemical Society), USDA Southern Regional Research Center (retired), ~42 attendees, developing biodegradable replacements for current petroleum-derived plastics, many younger people attending and Juan received several requests for the recording of the talk

Distinguished Scientist Award (DW, JS) – October 17, 2023, Distinguished Scientist Award Dinner, Understanding Protein Dynamics for Structure-based Drug Design: Design Stories of Crizotinib, Lorlatinib and Repotrectinib, Award Winner: Dr. Jean Cui, Scientific Founder, President and CEO at BlossomHill Therapeutics, Inc, 62 attended, photos on Google drive and will be published in Newsletter, presentation went well, sponsorship covered a portion of the costs

Chem Expo (JT) – 40 Scouts registered, announcement of potential prizes sent to local middle and high schools, Abbey Rentals price was good, maybe short some on number of volunteers; access to the venue at 8 a.m.

SABPA / ACS Seminar (DW) – Nov. 7, at Novartis, three speakers each addressing KRAS inhibitors, 168 registrants, Medicilon sponsoring so minimal expenses to SDACS or SABPA, doors open at 4, talks at 5, venue needs to be vacated by 8 p.m., Novartis crew will do all cleaning, some extra costs for one speaker's travel, alcoholic beverages will be available, Novartis requesting list of registrants for printing name tags, signs will be in place for parking

Paying Eventbrite (JGG) -- Eventbrite is charging for events having >29 registrants, pricing either \$80 / month or \$25 / event

Motion: allocate \$25 for Eventbrite to handle registration for Year-End Wrap-up -- **Approved**

Dropbox (JS) – Jim has been using a gratis Dropbox in the past or Google Drive but is requesting an Eventbrite business account to give members better access to records of Section activities, no discounts advertised on Website

Motion: Allocate \$240 / year for Dropbox business subscription to store photos, videos, records of Section events – **Approved**

Elections (JT) – Roster has been received, Jackie Trischman will send out the ballots electronically to conclude election before Dec. 1 deadline from National

By-laws Update (JGG) – National has sent us notification that the Section by-laws do not conform to National's requirements, suggestion to defer consideration of by-law changes until new ExComm in place in Jan.

MedChem Symposium (MT) – Proposing revisions from pre-COVID; sponsorships have covered costs when the event was in-person, new UCSD partner to potentially invigorate the committee, suggesting budgeting \$8K with the expectation that sponsorships will reimburse most or all of this seed fund, the committee is starting planning 2 months early because we have not had an in-person MedChem for several years

Motion: return Medchem in-person event and allocate \$8,000 as a seed fund --**Approved**

Year-end Wrap-Up (JS) – Dec. 7, planning for buffet / prime rib dinner at the Butcher Shop

Instituting New Awards (JGG) – Proposal for new awards not completed so no further discussion at this point

DEIR Proposal (CV) – Christina drafting proposal at this time

Adjourn: 8:02 p.m.

Next meeting: Dec. 7, @ Year-end meeting

These minutes have not been approved by the Executive Committee



The San Diego Section of the American Chemical Society would like to thank our Corporate Sponsors.

NON-PROFIT ORGANIZATIONS!

Does your non-profit organization have an upcoming event that might be of interest to members of the ACS – San Diego Section? If so, please send your announcement to our 2022 Chair, **Juan Gonzalez-Gonzalez** at jpgg@sandiegoacs.org. Once approved, Juan will see that your announcement is published on our website (www.sandiegoacs.org) and, if received by the 20th of the month before the event, in The San Diego Chemist newsletter. This is a free service of the ACS – San Diego Section. Take advantage of it!

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For more information, please contact:
Carolina Ibarra at cibarra@sandiegoacs.org

THE SAN DIEGO CHEMIST, the official newsletter of the San Diego Section of the American Chemical Society, published on a monthly basis, can be viewed at <http://www.sandiegoacs.org/newsletter/>. All contents are published at the discretion of the Section's Executive Committee. Events of interest to chemistry professionals in the community may be included in the events calendar as space permits and are subject to editing for brevity. Advertisements and announcements from the chemistry community are accepted at published rates. The deadline for items submitted is the 20th of the month for publication by the end of that month.

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ATTENTION COMPANIES!

Do you hire student workers?

If you have open positions in chemistry and biochemistry that would be of interest to college students, such as summer internship opportunities, here is a list of contacts you'll want to keep handy. The people listed below are the faculty advisors of the ACS Student Affiliate groups for all chemistry programs in San Diego County. These professors can get the word out to all chemistry and biochemistry majors at their schools about jobs, career fairs, open houses, etc.

California State University, San Marcos

Jacqueline Trischman
trischma@csusm.edu
760-750-4206

Point Loma Nazarene University

Laurance Beauvais
lbeauvais@pointloma.edu

San Diego Mesa College

Synthia Chang
schang001@sdccd.edu

San Diego Miramar College

Dr. Cynthia Gilley
cgilley@sdccd.edu
Dr. Janina Moretti
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Southwestern College, Chula Vista

Juan Gonzalez
jgonzalez3@swccd.edu
619-421-6700x5947

University of California, San Diego

Jeremy Klosterman
jkk@ucsd.edu

University of San Diego

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Chair-Elect			
Past Chair	Jim Shih, Eli Lilly & Co, jshih@sandiegoacs.org	(2023)	626-826-3561
Secretary	William Tolley, Seacoast Science, Inc., b_tolley@juno.com	(2023)	858-780-0978
Treasurer	Desiree Grubisha, Heron Therapeutics, desgrubisha@gmail.com	(2023)	858-254-5497

Councilors

Hui Cai, WuXi AppTec	(2025)	858-361-8838
Surya K. De, Conju-Probe	(2024)	858-337-4961
Desiree Grubisha, Heron Therapeutics	(2024)	858-254-5497
Valerie Kuck	(2023)	973-744-5510
Jackie Trischman, CSUSM	(2025)	858-414-3323
David Wallace, Wallace Scientific Consulting	(2024)	858-638-1866

Alternate Councilors

Julann Miller	(2023)	
Ben Pratt, Pratt Pharma Consulting LLC	(2025)	858-945-7893
Jim Shih, Eli Lilly & Co	(2024)	626-826-3561
Shannon Woodruff, HP Inc.	(2023)	949-735-9021

Members-at-Large

Sean Anderson, Application Specialist, 3M	(2024)	661-714-6174
James O'Brien, TE Connectivity	(2023)	858-336-0654
Bill Szabo	(2025)	858-550-0306
Christina Vialva, Southwestern College	(2024)	951-287-4503

STANDING & SPECIAL COMMITTEES**Awards Nomination Committee**

Valerie Kuck (Co-Chair)	973-744-5510
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ChemExpo

Jackie Trischman, CSUSM	858-414-3323
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Communications Committee

Surya K. De, Conju-Probe.	858-337-4961
Desiree Grubisha, Heron Therapeutics	858-254-5497
Ken Poggenburg	760-635-2573
Carolina Ibarra (Newsletter Editor & Social Media Manager)	619-618-9240
David Wallace, Wallace Scientific Consulting	858-638-1866

Distinguished Scientist Awards Nomination Committee

OPEN (Chair)	
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Barbara Sawrey	858-729-0689
David Wallace, Wallace Scientific Consulting	858-204-5412
Surya K. De, Conju-Probe	858-337-4961

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Joan Schellinger, USD	619-260-7960

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Ryan Smith	619-744-2220

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Ken Poggenburg	760-635-2573

Law Committee

Ryan C. Smith, Duane Morris LLP	619-744-2220
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MedChem Symposium

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Mark Tichenor (Co-Chair), Janssen Pharmaceuticals, Inc.
David Wallace (Co-Chair), Wallace Scientific Consulting

858-945-7893
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760-635-2573

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973-744-5510

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