MEDICINALCHEMISTRY

2020: A LOOK AHEAD

Part of Proventa International's U.S. Medicinal Chemistry Strategy Meetings 2019 InterContinental, San Francisco, CA - 29 October 2019 and Le Méridien, Cambridge, MA - 14 November 201

ATTENDEE STATISTICS - WHO WENT AND WHAT THEY'RE INVESTING IN

HIGHLIGHTS FROM ALL OUR TRACKS THIS YEAR

TOP STRATEGIC CHALLENGES FOR MEDICINAL CHEMISTRY, 2020 AND BEYOND

AN EXPERT LOOK AT THE NEXT FIVE YEARS IN MEDICINAL CHEMISTRY

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INTRODUCTION

Proventa's U.S. MedChem Meetings have just concluded for another year, showcasing the success of the company's innovative format: delegates and sponsors alike were pleased and surprised by the usefulness of Proventa's unique roundtable discussion format, the amount of connections made with peers and the seniority and experience of attendees present.

Discussions hit on the biggest topics of the moment, from the vast potential of AI and machine learning, to design and custom synthesis, to the search for suitable strategic partnerships and the challenges and solutions around process outsourcing.

THE FUTURE OF MEDICINAL CHEMISTRY

This report features a wealth of information for those who attended the 2019 strategy meetings and indeed those who did not, but more importantly looks beyond the event to the future: it contains not only statistics showing job titles and investments of this year's delegates, but highlights from the event talks themselves and our facilitators' impressions of how biomanufacturing will evolve and change over the next five years.

There is a wealth and variety of information packed into the pages of this report: we hope you find them of interest and use, and enjoy your time reading.

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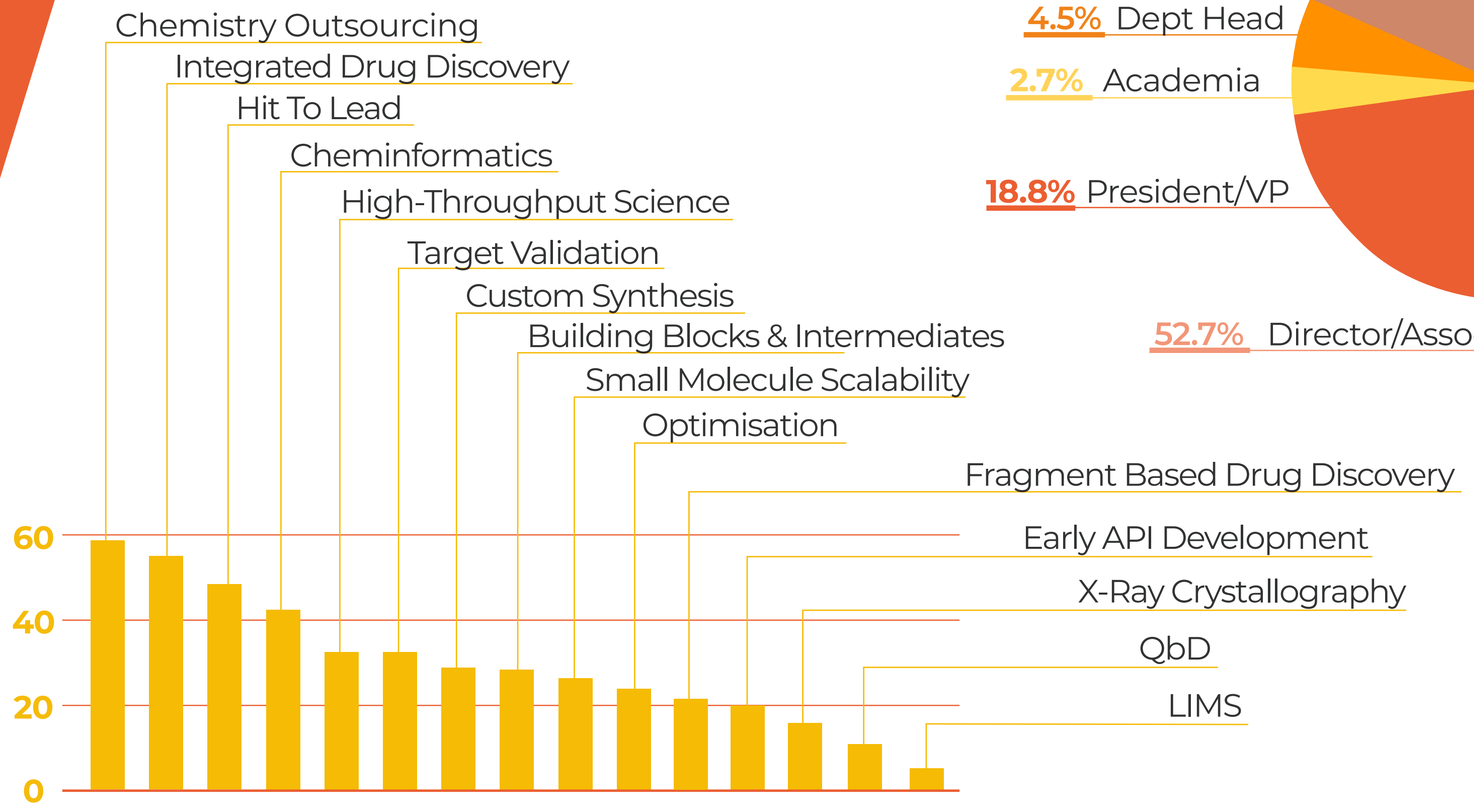
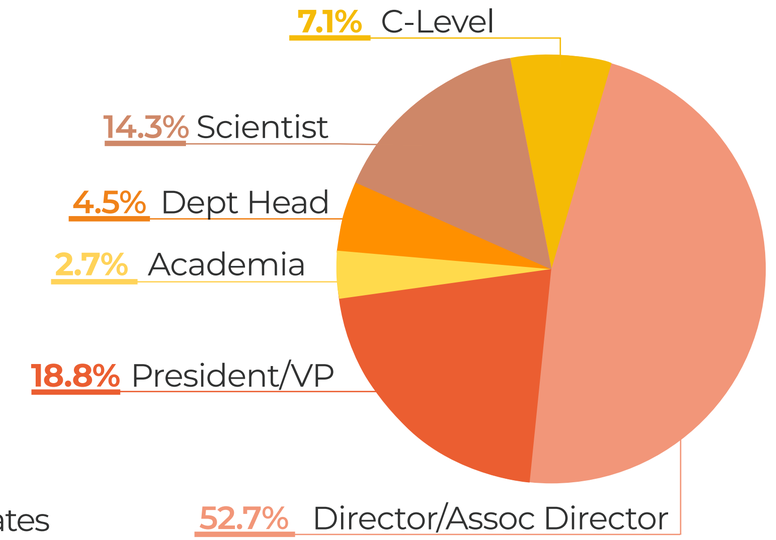
2019 DELEGATES BIGGEST INVESTMENTS



2019 ATTENDEE BREAKDOWN



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2 EVENT HIGHLIGHTS

The 2019 U.S. Medicinal Chemistry Strategy Meetings saw engaging roundtables across six main tracks, with everyone who attended finding something of use. The tracks were: AI/ML; design & custom synthesis; integrated drug discovery; strategic partnership & collaboration; chemical biology & cheminformatics; and hit-to-lead optimisation.

AI AND MACHINE LEARNING

The AI and ML track started with a discussion on the reality of AI versus the hype, led by Krista Goodman of GSK. It began with a mention of recent claims that a company had gone from paper to full drug in 42 days, which when examined further was not a novel drug at all: it was only two atoms away from an already marketed drug. The company had used generative modeling to train an AI to look at compounds and make predictions, but it was not entirely novel.

On the other side of the topic, a study was brought up in which scientists derived cellular phenotypes from images: what once took six months can now be done in an afternoon.

Delegates focused at the start of the session on the hype, agreeing that most molecules coming out of generative models were ineffective. They said that even should a company have access to a massive dataset, the right proportion of molecules must still be found, which can be extremely difficult. On top of this, delegates noted that most companies still do multi-object optimisation poorly.

Looking at the positives of AI and ML, the delegates noted that AI was definitely delivering in synthesis planning. Scaling is also less of an issue than it was - while you may need a billion molecules to synthesise, these can be analysed down to a few hits through a series of filters, one of which is generally a manual filter.

The next talk in the track focused on embracing the present and the future, in regards to digitisation of organic synthesis for drug discovery, run by John Wai of WuXi AppTec. The track ended with Patrick Walters of Relay Therapeutics discussing the mapping of AI's impact in the world of drug discovery.

DESIGN AND CUSTOM SYNTHESIS

The track on design and custom synthesis started with Darby Schmidt of Rheostat Therapeutics leading a roundtable on validating automated design and active learning, followed by a discussion on the scientific and operational aspects of getting leads through discovery and development by Tracy Brennan of Adesis.

After lunch, Abovchem's Barden Lee discussed reducing the delay from screening compounds to truckload, and Aminex Therapeutics' Mark Burns ended the track with a talk on exploring privileged scaffold in drug design and discovery.

INTEGRATED DRUG DISCOVERY

This track began with a roundtable on outsourcing integrated drug discovery projects, facilitated by Andrew Roughton of WuXi AppTec. After that, Gregory Bisacchi of Syngene International gave an excellent discussion on reducing discovery timelines.

This talk began with a look at some of the big bottlenecks in the pharma timeline, particularly around design and logistics. One delegate noted that a four-year study can in fact take five years due to logistics alone. The question was posed: if the process moves more quickly, are success rates better?

One solution posed around discovery was to think very carefully about your objectives and what you're trying to achieve before initiating any work: this could help cut out extraneous areas which delay the process as a whole.

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STRATEGIC PARTNERSHIP & COLLABORATION

The strategic partnership & collaboration track began with a discussion by Dennis Dean of IFM Therapeutics, who helped lead a talk on collaborations to address early safety assessment and mitigating risks in drug discovery. He was followed by Richard Soll of WuXi AppTec, leading the discussion on new mechanisms for enabling early-stage innovation.

After lunch, an excellent discussion on assisting delegates in accelerating their drug development programs was given by Satish Nagaraj of Jubilant Biosys. The track concluded with a roundtable on the physical properties and quantitative structure-activity relationships, facilitated by Blaise Lippa of Morphic Therapeutics.

CHEMICAL BIOLOGY AND CHEMINFORMATICS

The event's track on chemical biology and cheminformatics began with a talk on the use of targeted protein degradation strategies with small molecules, led fantastically by Jennifer Petter of Arrakis Therapeutics. Following this, Ted Suh of Orionis Biosciences spoke with delegates on methods to discover and characterise ligand-protein interactions.

After lunch, the final talk of the track focused on the future of collaborative drug discovery informatics, and was given by Peter Gedeck of CDD Vault.

HIT-TO-LEAD OPTIMISATION

This track began with a talk by Michael Luzzio of Skyhawk Therapeutics on how far drug-likeness prediction tools can be simplified. After that, Santosh Patil of Sai Life Sciences facilitated a roundtable on fragment-based drug discovery for hit identification and hit-to-lead optimisation, as well as lessons learned.

Much of the roundtable's focus revolved around the techniques and advantages of fragment-based chemical libraries over regular chemical libraries. The question was brought up of how to introduce SP3 carbon into fragment-based libraries. Delegates suggested to start simply, with more complexity introduced as more SP3 is added. Some delegates agreed on this as a better hit-finding approach compared with SP2, but others warned not to be too clever with the process: hits would be found no matter which process was used.

All agreed that patience was a priority when working with fragment-based drug discovery: it takes time, and depending on the target can take a long time to optimise.

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3 KEY DELEGATE CHALLENGES

One of the most important resources available to any senior figure in biotech or pharmaceuticals is an understanding not only of the field at present but where the field is going, and the key obstacles that any company in the sector faces.

Proventa International surveyed a number of major players in the field prior to our 2019 event, using expert opinion and insider knowledge to uncover out of the many obstacles on the horizon the major challenges to overcome in the next few years.

MAJOR CHALLENGES - 2020 AND BEYOND

TARGET IDENTIFICATION AND VALIDATION

By far the biggest challenge cited by delegates involved target identification and validation: among other issues, experts noted that finding and validating novel targets, determining how chemistry can assist novel target identification, accessing good high-quality tools for target validation and target validation for challenging GPCR targets were all difficult challenges to overcome in the next few years.

AI AND NEW TECHNOLOGY

The next most spoken-of challenge for the future involved new and innovative technologies, including AI and machine learning: experts set out that they were struggling with integrating AI into drug discovery, finding enabling technologies for “hard to drug” targets like PPIs, and even educating new users on innovative technologies being rolled out.

LEAD OPTIMISATION

Lead optimisation was another of the main challenges facing experts in the coming years: delegates surveyed suggested that present issues include lead optimisation to deliver preclinical candidates and active learning in lead optimisation.

SCIENTIFIC CHALLENGES

A wide range of general medical challenges were the next most challenging area for experts in medicinal chemistry today: technical issues ranging from compound mapping to peptide synthesis to compound attrition will be a considerable focus for scientists over the coming years.

OUTSOURCING AND PARTNERSHIPS

Outsourcing work is another major focus, according to the survey: delegates expressed concerns around outsourcing chemistry to third parties, and noted issues around finding good CROs and external parties to even conduct the work. Finding strategic partners for additional development and creation of new assays was also cited as a major challenge over the next few years.

ASSAY DEVELOPMENT

Assay development was considered a significant issue for the near future: delegates are looking to solve problems in early stage predictive assays for PK and toxicology; development of robust binding assays with poorly-behaved protein oligomers; and advanced cellular assays.

DRUG DISCOVERY

General drug discovery was next on the list of concerns for the near future: among other things, delegates suggested challenges around phenotypic discovery and optimisation; enabling NGS in-house and integrating it into drug discovery; enabling systems biology/bio-modeling capabilities in support of early drug discovery disease concepts; and reduction of turnaround time in discovery.

TRAINING AND HIRING STAFF

The hiring and training of internal staff was another issue facing medchem experts in the coming few years: finding the right staff with select skills is a difficulty many face.

FUNDRAISING AND COST

Completing initial fundraising and finding the necessary funds for further work were issues several delegates faced, with costs - such as cost of goods and general cost-efficiency - rounding out the financial challenges experts are currently thinking about.

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EXPERT OPINION ON THE FUTURE OF MEDICINAL CHEMISTRY

Evolutionary rather than revolutionary, innovation in medicinal chemistry is arriving as fast as in any other area of pharmaceutical science. The advancement of machine learning, greater business collaboration and improved molecular modelling through advances in computing have all been suggested as upcoming innovations in the space. To clarify the matter, and find out what people in the field itself think, we spoke to some of the experts and facilitators at our event to determine what the next five years really will bring to the practice of medicinal chemistry.

MACHINE LEARNING

One facilitator, a Head of Early Discovery, strongly stressed that machine learning would be one of the most important innovations in years to come. She suggested that with the technology's expansion, most field experts would need to quickly learn how to work with computers and begin to move away from traditional chemistry and making dozens of molecules.

She did note, however, that there is still significant misunderstanding in the sector around the use of machine learning: often, scientists ask how best to input medicinal chemistry into machine learning, missing the point that ML algorithms will learn by themselves, as the name suggests.

VIRTUAL LIBRARIES

Another facilitator noted that the creation of virtual libraries would massively help the sector, allowing scientists to use different tools, structures, and modelling to narrow down molecules without having to make so many. This could then allow better exploration of different protein targets, or any targets for the disease itself.

Despite this, they said new methods of chemistry development are still very important, with computers assisting in designing new, more powerful methodologies for making molecules.

VALIDATION TOOLS

A facilitator mentioned that the limitations inherent in target validation tools, such as CRISPR or RNA-Seq, are major barricades in the way of progress. Currently, professionals looking at a new target without a lot of known chemical information are working with older, traditional methods of validation, which can be difficult and time-consuming. Until the available tools improve, she said, the field of medicinal chemistry will not move at a swift rate towards innovation.

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