Breakthrough Technology Solving Characterization Challenges and Accelerating Biopharmaceutical Drug Development

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High-Resolution Ion Mobility Mass Spectrometry (HRIM-MS) has emerged as a promising new separations technique in the biopharmaceutical and clinical market. In this interview, **Dr. Melissa Sherman, CEO of MOBILion Systems Inc**., introduces us to MOBIE, MOBILion's first commercial product, which addresses characterization challenges faced during biopharmaceutical drug development and quality monitoring.

Why is there a need for HRIM in the biopharma market and how does MOBIE address this?

Generally speaking, classic separations techniques are too slow, too complicated, and often not powerful enough to address molecular and structural identification challenges adequately, and in a time frame in keeping with the fast pace of biologic drug development. High-Resolution Ion Mobility Mass Spectrometry (HRIM-MS) addresses these deficiencies, providing a tool for pharmaceutical companies to develop safer and more effective biologic therapeutics and aid academic researchers in discovering novel biomarkers.

HRIM-MS provides fast, efficient separations with superior resolution and reproducibility, quicker, simpler method development, and greater instrument uptime. HRIM separates ionized molecules in the gas phase and has sophisticated chemical and electronic properties that separate analytes with the same molecular mass more effectively by their shape, ion polarity and collision cross-section. MOBILion has introduced the first commercial HRIM platform – MOBIE. Integrated with Agilent Technologies' 6545 and

6545XT Q-TOF instruments, MOBIE enables fast, efficient high-resolution characterization of biologics. MOBIE addresses the challenges being faced in biopharmaceutical drug development, where there is a growing demand for higher-order instrumentation that can characterize more complex therapeutic systems and accelerate biomarker discovery.

What differentiates your HRIM technology from traditional separations methods?

HRIM is driven by Structures for Lossless ion Manipulation (SLIM) technology, originating from the laboratory of Dr. Richard D. Smith at Pacific Northwest National Laboratory. As an ion mobility research veteran, Dr. Smith was aware of the deficiencies with other ion mobility spectrometry (IMS) technologies first-hand and set out to overcome those with SLIM, providing an unprecedented capability to separate and identify molecular structures that are practically indistinguishable using established methods such as liquid chromatography (LC).

Unlike LC, which has hundreds of moving parts, HRIM has none. It is easier for a less skilled operator to set up, use the equipment and interpret the results so that scientists are able to run the instrument usually after only two days of training: greatly improving reliability and reproducibility in the lab.

The key differentiating factor with HRIM is that we are digitizing separations. While other ion mobility platforms are limited to a linear form factor and typically have big, ring electrodes with a minimal path length of around 1 meter, our separations are achieved on printed circuit boards (PCBs), and electrode patterns unique to SLIM technology can send ions around corners. This allows us to break linear path boundaries and fit 13m of path length into a small compact instrument that is only 14x18 inches. A longer path length enables the separation of molecules with very minor differences, making MOBIE's analysis very high resolution.

Incumbent techniques for separating ionized molecules are often a trade-off between ease-of-use, throughput, or resolution.

MOBIE is a next-generation separations technology because it sufficiently provides all three simultaneously, so researchers don't have to choose. It can separate any analyte type on its PCB, improving throughput and making it more accessible to users who no longer need to change columns. This allows biopharma and clinical researchers to either separate and identify molecules that were previously indistinguishable using other techniques or separate familiar molecules much faster and more

easily.

Can you talk about the applications within biopharma that MOBIE has shown promise in so far?

We're working with our biopharma customers to address the deficiencies in the characterization of protein-based therapeutics to get drugs to market faster and to better characterize biologics, whether it be peptide mapping, glycan analysis or intact protein subunit analysis. We accelerate critical quality attribute (CQA) workflows while providing the deeper and higher resolution information that is crucial for the development of stable and effective biotherapeutics.

We are excited to have systems out in the field with our beta users and key collaborators. Our goal is to address workflows in the characterization of biologics; to improve the speed and efficiency with which we identify Critical Quality Attributes (CQAs) in routine assays, but also to extend into addressing the characterization of challenging molecules such glycans and glycopeptides – classes of molecules that are critical in the development of next generation therapeutics. We have collaborated with Janssen Pharmaceuticals to complete rapid glycan analyses: HRIM-MS has shown tremendous potential for seamless separation of glycans and the careful monitoring of protein glycosylation. A standard LC-MS based workflow can range from 15 to 30 minutes but, with HRIM, we are able to see all the glycans of interest in a two-minute analysis time. In this case, not only did we see a tremendous increase in throughput, but we were able to increase the identification of glycans of interest from 53% with the HILIC-based method, to 100% with HRIM enabled.

We've also been working with the Biopharmaceutical Analysis Training Lab (BATL) at Northeastern University, identifying post-translational modifications (PTMs) at the amino acid level. Typically, using LC-MS comes at the expense of analysis time, with a typical peptide mapping workflow taking 90-minutes and there is a substantial risk of under-reporting. With MOBIE, we are breaking through the threshold of characterization that exists today because we can provide the resolution to identify PTMs on proteins and peptides that other instruments fail to detect. Using HRIM, we can take the workflow time down to 5-10 minutes and can recognize mass-neutral PTMs, such as deamidations, that other workflows would fail to detect in that time frame. This minimizes the risk for pharmaceutical manufacturers of under-reporting key PTMs that impact the safety and efficacy of drugs in development.

Now that you have commercially launched MOBIE, what is the next phase of development for MOBILion Systems?

The great thing about our HRIM technology is that it is uniquely tunable and customizable. By changing the electrode pattern and the control electronics, we have a “smart” technology that is able to manipulate ions in nearly endless combinations and permutations, enabling us to develop fit-for-purpose concepts.

The next phase of development for us is focused on a standalone concept, which is the same SLIM separations chamber with an onboard embedded detector, but it will not have to be integrated with a third-party mass spec. The same enabling technology, delivered in a standalone, easier to use, targeted analysis form factor, provides us with access to clinical diagnostic markets and early disease detection markets. For example, in a pharmaceutical QC lab, or in a diagnostic lab, where analysis is very targeted, you do not need the mass spectrometer to give that additional information. We can do the identification just from this lens separation alone. We are already paving the way for the translation of the discoveries in the pharmaceutical and academic labs, and into the diagnostic markets.

Now that we have launched this game-changing technology, we are confident that it is going to have a major impact on the biopharmaceutical quality monitoring and omics translational research markets.

Keep an eye out for news and developments on the website at www.mobilionsystems.com or connect with us on LinkedIn.