

# PROTEOME SCIENCES plc

## PRESS RELEASE

For immediate release

27 November 2007

### **OVERCOMING THE BIOMARKER VALIDATION BOTTLENECK USING TANDEM MASS TAG (TMT<sup>®</sup>) WORKFLOWS AND APPLICATIONS**

#### ***Proteome Sciences introduces Tandem Mass Tag (TMT<sup>®</sup>) labelling***

Proteome Sciences plc, a global leader in applied proteomics, has developed and launched a range of ground breaking isobaric mass tagging reagents, Tandem Mass Tags (TMT<sup>®</sup>), with workflows and applications that will transform the discovery, validation and routine measurement of protein biomarkers by mass spectrometry. The TMT<sup>®</sup> products provide novel time- and cost-effective alternatives to the challenge of immunoassay development, radically reducing the development time for biomarker assays. These features address the increasing requirements of the global regulatory system, led by the FDA in the USA, to use biomarkers and biomarker data to accelerate and improve drug development and to support the advances in personalised medicine.

With global patents recently issued covering the field of isobaric mass tagging, Proteome Sciences has developed TMT<sup>®</sup> to meet the needs for fast, flexible and cost efficient workflows for biomarker discovery and validation. These provide improved precision, performance and accuracy of quantitation of any proteins in a sample by mass spectrometry. In addition, TMT<sup>®</sup> can be used with established protein biomarkers to diagnose disease and in pharmaceutical development, to assess drug safety, efficacy and patient stratification.

Specific applications have been developed for two key areas of unmet need:

**TMT<sup>™</sup>calibrator**, enables the absolute quantitation of multiple biomarker proteins in a single experiment by providing multipoint calibration curves for all proteins of interest, analogous to more traditional ELISAs;

**TMT<sup>®</sup> Reference Materials** allow the accurate relative quantitation of hundreds of proteins in large and complex biomarker programs, providing reliable comparison across different laboratories or at different times.

Customers can access the full range of customised TMT<sup>®</sup> labelling through the ProteoSHOP<sup>®</sup> services provided by Proteome Sciences in its London, UK and Frankfurt, Germany laboratories.

*Commenting Ian Pike, Chief Business Officer of Proteome Sciences said:*

“Pharmaceutical and diagnostic companies, academic researchers, CRO’s, charities and other researchers who need to discover and validate protein biomarkers or wish to rapidly develop multiplex assays can now use TMT<sup>®</sup> workflows. These will radically reduce the time and costs, allowing for highly improved success rates.”

“Customised TMT<sup>®</sup> labelling offers a valuable addition to the range of ProteoSHOP services which combine to provide the most advanced workflows and applications in protein biomarker discovery and validation and are already being provided to our clients. TMT<sup>®</sup> method development kits are also available, containing the necessary reagents for customers to quickly adapt their internal workflows. Further kits including TMTsixplex<sup>™</sup> and various TMTcalibrator<sup>™</sup> assays and TMT Reference Materials<sup>™</sup> will be accessible through our TMT<sup>®</sup> licencees”

*Christopher Pearce, Chief Executive of Proteome Sciences, added:*

“Whilst the discovery and validation of biomarkers is currently a very time consuming and costly exercise, they are increasingly becoming an essential requirement for the development of novel diagnostic and prognostic assays and for determining the efficacy and safety of new drugs. Our ProteoSHOP workflows using TMT<sup>®</sup> overcome these major bottlenecks in a time- and cost-efficient way by removing the need to develop and validate antibody-based immunoassays. Instead of taking several years for the antibody-based assays, TMTcalibrator<sup>™</sup> assays can be developed in weeks”

“In short, we have developed TMT<sup>®</sup> to overcome the biomarker validation bottleneck and offer our customers simple workflows adapted to their needs and that provide high quality data on the already well established and rapidly expanding mass spectrometry user base.”

**## ends ##**

## **Notes to editors**

### **The Importance of Biomarkers in Healthcare – Focusing on the individual**

It is widely recognised that the established methods of drug development are becoming increasingly less able to deliver highly effective and safe new medicines, particularly for challenging diseases such as cancer and neurodegeneration. More stringent regulatory hurdles and a move to more chronic diseases means that the attrition rate of drugs failing in clinical trials is increasing rather than decreasing. At the same time there is a growing recognition that for many patients their current treatments are either completely ineffective or are only partially effective at the approved dose.

To improve on this situation, and to attempt to meet the potential offered by personalised medicine, pharmaceutical and diagnostics companies and their respective regulators are turning to biomarkers as objective measures of drug efficacy and safety. The discovery and validation of biomarkers is however, a long and expensive endeavour that until recently has been seen as more a barrier to drug development than as an aid to faster, cheaper and more successful pipelines.

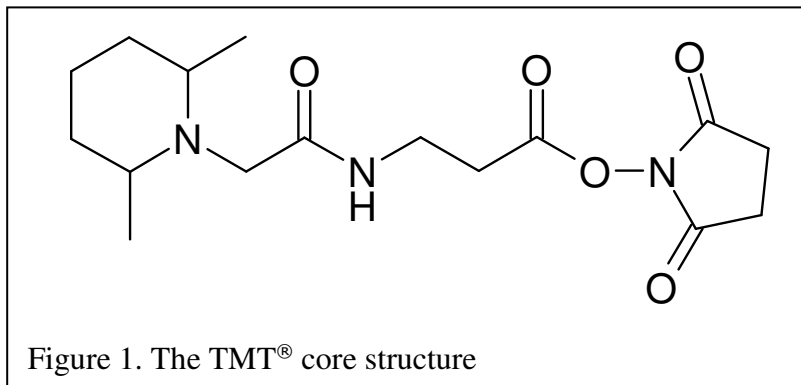
There is a challenge therefore, to provide improved methods for the timely discovery and validation of biomarkers during pre-clinical and first-in-man (Phase 1) trials and that can be adapted to deliver highly accurate and reproducible assays suitable for routine use in thousands of patients in late clinical studies (Phase3) and in routine patient management.

### Tandem Mass Tags – Novel Reagents for Biomarker Workflows

Tandem Mass Tags<sup>®</sup> belong to the family of reagents known as isobaric mass tags. As the term suggests, several different forms of a molecule have the same mass and can be independently attached to a peptide or protein via a reactive group. Two core elements, the Mass Reporter and the Mass Normaliser (Fig. 1), are connected via a Cleavable Linker, which has the tendency to break preferentially during MS/MS fragmentation conditions. By selective placement of isotopes such as <sup>13</sup>C, <sup>15</sup>N or <sup>18</sup>O at certain positions of the Mass Reporter or the Mass Normaliser, the mass of the respective core elements is varied to produce series of Mass Reporters, typically in 1 Dalton increments. To maintain the same mass of the TMT<sup>®</sup>, the absolute number of isotopes in a set of tags is kept constant.

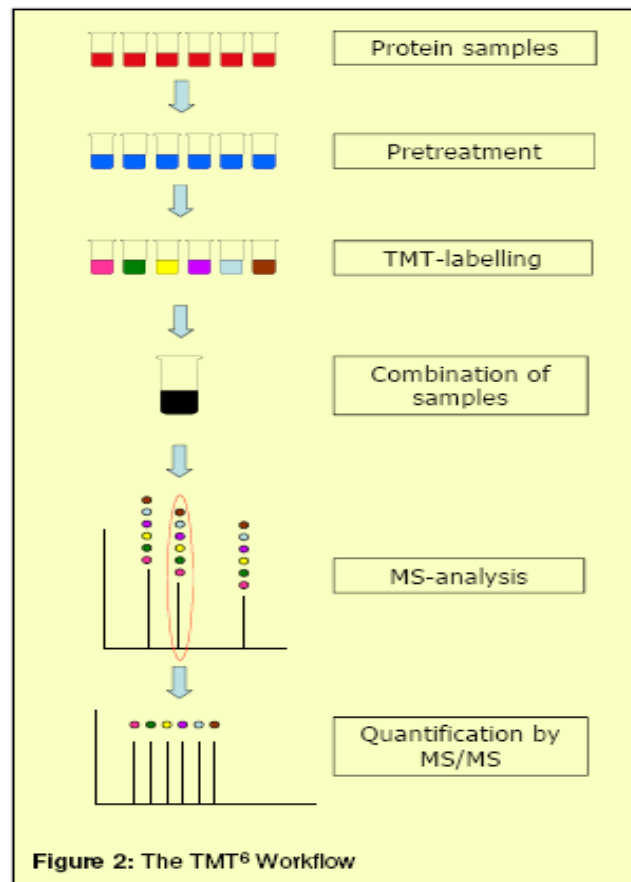
A range of TMT<sup>®</sup> products sharing an identical chemical structure (Fig. 1) have been developed for a wide range of research applications. TMTduplex<sup>™</sup> (TMT<sup>2</sup>) is designed for labelling and mixing of two samples and the TMTsixplex<sup>™</sup> (TMT<sup>6</sup>) for the labelling and mixing of up to six samples. Proteome Sciences also provide TMTzero<sup>™</sup> (TMT<sup>0</sup>) for all types of method development prior to the use of the TMT<sup>2</sup> or TMT<sup>6</sup> products. TMTcalibrator<sup>™</sup> has been developed based on TMT<sup>6</sup> for absolute quantitation of biomarker candidates against multipoint standard curves.

Whichever TMT<sup>®</sup> product is selected, the yield in MS/MS identifications is improved by ~ 25% compared to normal MudPIT-type experiments. For further improvement of proteomics workflow performance, TMT<sup>®</sup>-labelled biological reference materials from plasma and other body fluids will shortly be available.



When proteins from a sample have been labelled with a TMT<sup>®</sup>, they carry a distinct Mass Reporter which is specific for the labelled sample. Since a set of TMT's<sup>®</sup> will release a set of Mass Reporters, different protein samples can be mixed after first being individually labelled with a specific member of a TMT<sup>®</sup> set. Since all Tags of a set are identical in their chemical structure, they affect the physicochemical properties of any given tagged protein in exactly the same way.

The quantitative ratio of a protein between the mixed samples is therefore conserved during the entire workflow (Figure 2). Proteins will co-elute perfectly during chromatography, co-migrate on gels, and no pre-analytical procedures performed after mixing will affect the initial relative abundance ratio. If measured in a mass spectrometer in MS mode, only one peak is observed for each peptide. If the peptide is now selected for fragmentation in a MS/MS experiment, the Mass Reporter is released and shows a specific signal in a silent region of the mass spectrum. The ratio of different reporter ions is then used for quantitation.



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