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**HEALTH CANADA APPROVES FIRST RECOMBINANT HUMAN THROMBIN  
SURGICAL HEMOSTATIC SOLUTION**

**RECOTHROM<sup>®</sup> provides an aid to hemostasis on demand,  
allowing surgeons to deal with bleeding and complete the surgical procedure**

**TORONTO, ON – March 1, 2010** – Bayer HealthCare Pharmaceuticals announced today that RECOTHROM<sup>®</sup> (Thrombin alfa [Recombinant]), the first recombinant, plasma-free thrombin approved by Health Canada, is now available for use as a topical hemostatic solution. According to a recent clinical study, RECOTHROM<sup>®</sup> was found to successfully stop 80 per cent of surgical bleeding within three minutes and 95 per cent of bleeding within 10 minutes.<sup>1</sup>

“Perioperative bleeding remains a significant issue in cardiac surgery as it is associated with an increased mortality, increased intensive care unit stay as well as increased morbidity in patients who suffer from that condition,” said Dr. Mackenzie Quantz, Associate Professor, Cardiac Surgery, Surgical Director of Heart Transplantation, London Health Sciences Centre.

“RECOTHROM<sup>®</sup> is a valuable addition to our existing surgical tools and is especially useful for patients with diffuse oozing from raw surface tissue. Because RECOTHROM<sup>®</sup> is a recombinant product, there is very low risk of immunogenicity which is especially important in our cardiac patients because of the risk of re-operation,” added Dr. Quantz.

“Based on a clinical trial, surgeons will find RECOTHROM<sup>®</sup> to be a convenient surgical hemostat. RECOTHROM<sup>®</sup> is easy to prepare and use. It requires no refrigeration and can be stored in the operating room. When reconstituted, it can be kept up to 24 hours for lengthy surgical procedures. The components are latex-free and the needle-free transfer device eliminates the risk of needlesticks<sup>2</sup>,” said Shurjeel Choudhri, MD, Senior Vice President and Head, Medical and Scientific Affairs, Bayer Inc.

RECOTHROM<sup>®</sup> is intended for topical use only.<sup>3</sup> It may be applied directly to the bleeding site, or used in conjunction with a compatible absorbable gelatin sponge to promote hemostasis. When RECOTHROM<sup>®</sup> solution comes into contact with blood it helps clotting.<sup>4</sup>

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<sup>1</sup> Chapman WC, Singla N, Genyk Y, McNeil JW, Renkens KL, Jr., Reynolds TC, et al. A phase 3, randomized, double-blind comparative study of the efficacy and safety of topical recombinant human thrombin and bovine thrombin in surgical hemostasis. J Am Coll Surg 2007;205(2):256-65.

<sup>2</sup> Product Monograph, December 15, 2009, Page 18.

<sup>3</sup> Product Monograph, December 15, 2009, Page 7.

<sup>4</sup> Product Monograph, December 15, 2009, Page 18.

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## About RECOTHROM<sup>®</sup>

RECOTHROM<sup>®</sup> is a new topical hemostatic agent with versatile delivery options for use in oozing blood and minor bleeding. It is indicated as an aid to hemostasis whenever oozing blood and minor bleeding from capillaries and small venules is accessible and control of bleeding by standard surgical techniques is ineffective or impractical.

The effectiveness of RECOTHROM<sup>®</sup> was evaluated in surgical settings where adjuncts to hemostasis are frequently required: hepatic resection, peripheral arterial bypass surgery, arteriovenous graft formation for hemodialysis access, and spinal surgery. The evidence to support the effectiveness of RECOTHROM<sup>®</sup> was not established in spinal surgery.<sup>5</sup>

Delivery options include using RECOTHROM<sup>®</sup> alone or with a compatible absorbable gelatin sponge. It is supplied as a lyophilized powder and sterile diluent for reconstitution in single use, preservative-free vials of 6,000 IU or 24,000 IU.<sup>6</sup> The volume of reconstituted RECOTHROM<sup>®</sup> required will vary, depending on the size and number of bleeding sites to be treated and the method of application. RECOTHROM<sup>®</sup> is convenient to store, can be reconstituted at room temperature, and is easy to prepare and use. Its needle-free transfer device eliminates the risk of needlesticks.<sup>7</sup>

RECOTHROM<sup>®</sup> is thrombin that has been developed in a laboratory<sup>8</sup> via recombinant DNA technology.<sup>9</sup> It is identical in amino acid sequence, and is structurally similar to naturally occurring human thrombin. The cell line used to manufacture RECOTHROM<sup>®</sup> has been extensively tested and shown to be free of known infectious agents.<sup>10</sup> It is not derived from animal or human blood, and contains no added human or animal components. RECOTHROM<sup>®</sup> is inherently free from the risk of transmission of human-borne pathogens, such as HIV, hepatitis, parvovirus, and the infectious agents associated with Creutzfeldt-Jakob Disease (CJD) and variant CJD.<sup>11</sup>

RECOTHROM<sup>®</sup> has low immunogenicity with a significantly lower rate of specific anti-product antibody formation than treatment with bovine thrombin. After surgery, only 1.5 per cent of RECOTHROM<sup>®</sup> patients developed antibodies.<sup>12</sup> It can be used safely in patients with pre-existing anti-thrombin antibodies to bovine thrombin preparations.<sup>13</sup>

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<sup>5</sup> Product Monograph, December 15, 2009, Page 3.

<sup>6</sup> Product Monograph, December 15, 2009, Page 3.

<sup>7</sup> Product Monograph, December 15, 2009, Page 18.

<sup>8</sup> Product Monograph, December 15, 2009, Page 18.

<sup>9</sup> Product Monograph, December 15, 2009, Page 3.

<sup>10</sup> Product Monograph, December 15, 2009, Page 3.

<sup>11</sup> Product Monograph, December 15, 2009, Page 3.

<sup>12</sup> Chapman WC, Singla N, Genyk Y, McNeil JW, Renkens KL, Jr., Reynolds TC, et al. A phase 3, randomized, double-blind comparative study of the efficacy and safety of topical recombinant human thrombin and bovine thrombin in surgical hemostasis. *J Am Coll Surg* 2007;205(2):256-65.

<sup>13</sup> Singla NK, Ballard JL, Moneta G, Randleman CD, Jr., Renkens KL, Alexander WA. A phase 3b, open-label, single-group immunogenicity and safety study of topical recombinant thrombin in surgical hemostasis. *J Am Coll Surg.* 2009;209(1):68-74.

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## **RECOTHROM<sup>®</sup> Clinical Trial Results**

A phase III multiple-site, randomized, double-blind controlled study was conducted to evaluate the comparative efficacy, safety and immunogenicity of RECOTHROM<sup>®</sup> and bovine thrombin in combination with an absorbable gelatin sponge as adjuncts to hemostasis in surgery. Efficacy was evaluated by the incidence of hemostasis within 10 minutes.<sup>14</sup> RECOTHROM<sup>®</sup> was found to successfully stop 80 per cent of surgical bleeding within three minutes and 95 per cent of bleeding within 10 minutes.<sup>15</sup>

The study was a multiple-site, randomized, double-blind controlled evaluation of RECOTHROM<sup>®</sup> compared with bovine thrombin, each at a nominal concentration of 1000 IU/ml. The study was conducted in 411 patients undergoing surgery in one of four surgical settings: spinal surgery, hepatic resection, peripheral arterial bypass surgery, and arteriovenous graft formation for hemodialysis access.<sup>16</sup> The evidence to support effectiveness of RECOTHROM<sup>®</sup> was not conclusively established in spinal surgery.<sup>17</sup>

The safety profile of RECOTHROM<sup>®</sup> was similar to that of bovine thrombin. Most adverse events were moderate in severity. The most common adverse events reported in both treatments were incision site complication (63% for both treatment groups), procedural pain (RECOTHROM<sup>®</sup> 29%; bovine thrombin 34%), and nausea (RECOTHROM<sup>®</sup> 28%; bovine thrombin 35%).<sup>18</sup>

## **About Bayer Inc.**

Bayer Inc. (Bayer) is a Canadian subsidiary of Bayer AG, an international research-based group with core businesses in health care, crop science and innovative materials. Headquartered in Toronto, Ontario, Bayer Inc. operates the Bayer Group's HealthCare and MaterialScience businesses in Canada. Bayer Crop Science Inc., headquartered in Calgary, Alberta operates as a separate legal entity in Canada. Together, the companies play a vital role in improving the quality of life for Canadians – producing products that fight diseases, protecting crops and animals, and developing high-performance materials for applications in numerous areas of daily life. Canadian Bayer facilities include the Toronto headquarters and offices in Montréal and Calgary.

Bayer Inc. has approximately 900 employees across Canada and had sales of \$908 million CDN in 2008. Globally, the Bayer Group had sales of over 32 billion Euro in 2008. Bayer Inc. invested approximately \$36 million CDN in research and development in 2008. Worldwide, the Bayer Group spent the equivalent of over 2.6 billion Euro in 2008 in R&D. For more information, go to [www.bayer.ca](http://www.bayer.ca).

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<sup>14</sup> Product Monograph, December 15, 2009, Page 12.

<sup>15</sup> Chapman WC, Singla N, Genyk Y, McNeil JW, Renkens KL, Jr., Reynolds TC, et al. A phase 3, randomized, double-blind comparative study of the efficacy and safety of topical recombinant human thrombin and bovine thrombin in surgical hemostasis. *J Am Coll Surg* 2007;205(2):256-65.

<sup>16</sup> Product Monograph, December 15, 2009, Page 12.

<sup>17</sup> Product Monograph, December 15, 2009, Page 3.

<sup>18</sup> Product Monograph, December 15, 2009, Page 5.

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## **Forward-Looking Statements**

This news release may contain forward-looking statements based on current assumptions and forecasts made by Bayer Group or subgroup management. Various known and unknown risks, uncertainties and other factors could lead to material differences between the actual future results, financial situation, development or performance of the company and the estimates given here. These factors include those discussed in Bayer public reports which are available on the Bayer website at [www.bayer.com](http://www.bayer.com). The company assumes no liability whatsoever to update these forward-looking statements or to conform them to future events or developments.

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