**Supplementary Material**

1 Supplementary Figures and Tables

1.1 Supplementary Tables

**Supplementary Table 1.** List of primers used for the methylation analysis of *WNT1* by ddPCR.

| Assay  | Primers/Probe | 5’-Sequence-3’                      |
|--------|---------------|------------------------------------|
|        | Forward       | GAGGGGTAGTTTTTTTT                  |
|        | Reverse       | TCTAATTAAACAACCTAAAA               |
|        | Probe (FAM)   | GATCGAGTATGTGT                     |
| WNT1-M |               |                                    |
|        | Forward       | GAGGGTAGTTTTTTTT                  |
|        | Reverse       | TCTAATTAAACAACCTAAAA               |
|        | Probe (HEX)   | GGATTGAGTATGTGT                    |
**Supplementary Table 2.** Clinical characteristics of metastatic patients with luminal B breast cancer included in the study.

| Characteristics             | Patients (n=9) |
|-----------------------------|---------------|
|                             | No. | %   |
| **Age (years)**             |     |     |
| <65                         | 3   | 33  |
| 65-75                       | 3   | 33  |
| >75                         | 3   | 33  |
| **Immunohistochemistry**    |     |     |
| PR+                         | 8   | 89  |
| ER+                         | 9   | 100 |
| HER2+                       | 2   | 22  |
| Ki-67 ≥ 20%                 | 9   | 100 |
| **Histology**               |     |     |
| Ductal                      | 9   | 100 |
| **Stage**                   |     |     |
| IV                          | 9   | 100 |
| **Metastatic sites**        |     |     |
| 1                           | 4   | 44  |
| 2                           | 2   | 22  |
| 3                           | 3   | 33  |
| **Metastatic location**     |     |     |
| Visceral                    | 6   | 66  |
| Bone                        | 4   | 44  |
1.2 Supplementary Figures

**Supplementary Figure 1.** The genes of the 34 DMCpGs related to the Wnt signaling pathway belong to a functional network significantly enriched in protein interactions (P<0.001).
Supplementary Figure 2. Expression of \textit{WNT1} in primary luminal B breast tumors. Gene expression levels of \textit{WNT1} available in primary tumors of luminal B breast cancer patients (n=122) and nontumor controls (n=67) obtained by RNA-seq from TCGA. Expression levels are represented as the mean ± SEM.

Supplementary Figure 3. Methylation status of \textit{WNT1} in primary tumors of breast cancer subtypes (LABC, n=358; LBBC, n=122; TNBC, n=87; HER2+, n=17) and nontumor controls (n=79) from TCGA. Methylation data have been obtained from EPIC array analysis considering all TNM stages together (stages I-IV). Ctrl, control; P, p-value. LABC, luminal A breast cancer; LBBC, Luminal B breast cancer; TNBC, triple negative breast cancer; HER2+, HER2-positive.