



- (51) **International Patent Classification:**
A61K 38/00 (2006.01) C07K 14/50 (2006.01)
- (21) **International Application Number:**
PCT/US2015/057228
- (22) **International Filing Date:**
23 October 2015 (23.10.2015)
- (25) **Filing Language:** English
- (26) **Publication Language:** English
- (30) **Priority Data:**
- | | | |
|------------|------------------------------|----|
| 62/068,523 | 24 October 2014 (24.10.2014) | US |
| 62/068,514 | 24 October 2014 (24.10.2014) | US |
| 62/068,526 | 24 October 2014 (24.10.2014) | US |
| 62/068,534 | 24 October 2014 (24.10.2014) | US |
| 62/068,296 | 24 October 2014 (24.10.2014) | US |
| 62/141,337 | 1 April 2015 (01.04.2015) | US |
| 62/141,383 | 1 April 2015 (01.04.2015) | US |
- (71) **Applicant:** BRISTOL-MYERS SQUIBB COMPANY
[US/US]; Route 206 & Province Line Road, Princeton,
New Jersey 08543 (US).
- (72) **Inventors:** MORIN, Paul E.; Route 206 & Province Line
Road, Princeton, New Jersey 08543 (US). COHEN,

Daniel; Route 206 & Province Line Road, Princeton, New
Jersey 08543 (US). MUKHERJEE, Ranjan; 40 Brown
Drive, Churchville, Pennsylvania 18966 (US). REILLY,
Timothy P.; Route 206 & Province Line Road, Princeton,
New Jersey 08543 (US). CHRISTIAN, Rose C.; Route
206 & Province Line Road, Princeton, New Jersey 08543
(US). LIPOVSEK, Dasa; 100 Beaver Street, Waltham,
Massachusetts 02453 (US). CAMPHAUSEN, Ray; 100
Beaver Street, Waltham, Massachusetts 02453 (US). KRU-
PINSKI, John; 311 Pennington-Rocky Hill Road, Bldg.
21, Pennington, New Jersey 08534 (US).

(74) **Agents:** TESKIN, Robin L. et al.; LECLAIR RYAN,
P.C., Intellectual Property Department, 2318 Mill Road,
Suite 1100, Alexandria, Virginia 22314 (US).

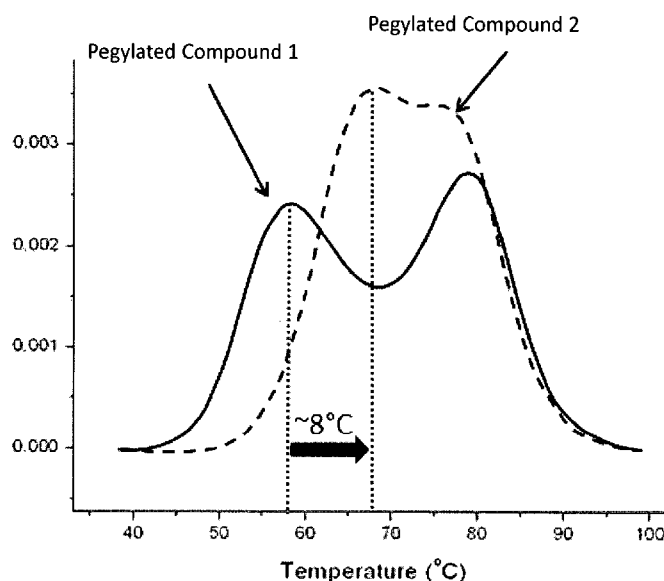
(81) **Designated States** (unless otherwise indicated, for every
kind of national protection available): AE, AG, AL, AM,
AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY,
BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM,
DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT,
HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR,
KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG,
MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM,
PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC,

[Continued on next page]

(54) **Title:** MODIFIED FGF-21 POLYPEPTIDES AND USES THEREOF

FIG. 3

Differential Scanning Calorimetry (DSC)



(57) **Abstract:** Modified FGF-21 polypeptides and uses
thereof are provided, for example, for the treatment of dis-
eases associated with fibrosis. Modified FGF-21 poly-
peptides are disclosed that contain an internal deletion and
optionally replacement peptide, optionally modified with at
least one non-naturally-encoded amino acid, and/or option-
ally fused to a fusion partner.



SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

- (84) Designated States** (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

Declarations under Rule 4.17:

- as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii))

— of inventorship (Rule 4.17(iv))

Published:

- with international search report (Art. 21(3))
— before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))
— with sequence listing part of description (Rule 5.2(a))

(88) Date of publication of the international search report:

16 June 2016