LETTER TO THE EDITOR

# Gene expression profile of adult T-cell leukemia/lymphoma with human T-cell lymphotropic virus type 1-infected Hodgkin and Reed-Sternberg-like cells is more similar to classic Hodgkin lymphoma than typical adult T-cell leukemia/lymphoma

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**Supplementary Table 1 Clinicopathological characteristics of ATLL-HH, CHL and typical ATLL**

**1A. Clinicopathological characteristics of ATLL-HH**

| Case no. | Clinical characteristics | | | | | | | | Pathological characteristics of HRS-like cells | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Age (years)/sex | Background status | Ann Arbor stage | LDH, U/L | sIL-2R, U/mL | Alb, g/dL | Ca, mg/dL | Extranodal involvement | Histology | CD30 | CD15 | PAX5 | BOB1 | OCT2 | CD3 | CD20 | CD5 | CD7 | TIA-1 | CD4 | HBZ-ISH | EBER-ISH | TRG |
| 1[a] | 69/M | Smoldering type[b] | IV | 332 | 6502 | 3.6 | 11.7 | Skin, Spleen, BM | MC like | + | + | - | - | - | - | - | - | - | - | +, f | + | - | polyclonal |
| 2 | Recurrent case of no. 1 (two years later) | NA | NA | 156 | 31911 | 1.6 | 8.9 | NA | MC like | + | + | - | NA | NA | - | - | - | - | NA | +, f | + | - | NA |
| 3 | 55/M | HTLV-1 carrier | I | 255 | 4667 | 4.4 | 8.9 | None | MC like | + | + | - | - | - | - | - | NA | - | - | + | + | - | polyclonal |
| 4[a] | 79/F | HTLV-1 carrier | IV | 331 | 7618 | 2.2 | 7.9 | Liver, Spleen, Bone | MC vs. NS | + | +, f | - | - | - | - | - | - | - | - | - | + | - | polyclonal |
| 5[a] | 80/F | HTLV-1 carrier | II | 307 | 9240 | 3.6 | 8.6 | None | MC like | + | +, f | - | - | - | - | - | - | - | - | - | + | - | NE |
| 6[a] | 72/F | HTLV-1 carrier | II | 299 | 2493 | 2.9 | 8.7 | None | MC like | + | +, f | - | - | - | - | - | - | - | - | + | + | - | clonal[c] |
| 7[a] | 81/M | HTLV-1 carrier | III | 465 | 34772 | 2.5 | 7.5 | Spleen | MC like | + | +, f | - | - | - | - | - | - | - | - | +, f | + | - | clonal[c] |
| 8 | 70/F | HTLV-1 carrier | IV | 306 | 4294 | 2.5 | 8.1 | BM, Liver, Spleen | MC like | + | + | - | - | | - | - | - | - | - | + | + | - | clonal[c] |
| 9[a] | 79/F | HTLV-1 carrier | IV | 306 | 4294 | 3.7 | 9.0 | Spleen, Bone | MC like | + | + | - | - | - | - | - | - | - | - | - | + | - | polyclonal |
| 10[a] | 75/M | HTLV-1 carrier | II | 197 | 1166 | 3.7 | 9.7 | None | MC like | + | + | + | - | +, f | - | - | - | - | - | +, f | + | - | clonal[c] |
| 11 | 65/F | HTLV-1 carrier | IV | 232 | 5403 | 3.7 | 8.8 | Spleen, Bone | MC like | + | +, f | + | + | +, f | - | - | NA | NA | NA | +, f | + | - | polyclonal |
| 12 | 82/M | HTLV-1 carrier | II | 200 | 1375 | 3.6 | 8.8 | None | MC like | + | + | +, f | - | - | - | - | NA | NA | - | - | + | - | clonal[c] |

All ATLL-HH cases were serological HTLV-1(+).

[a]Validated by immunohistochemistry of CCL17, pSTAT6, TBET, and IDO1.

[b]10 years prior to the diagnosis of ATLL-HH.

[c]Monoclonal peak was identified with polyclonal backgrounds.

Alb, albumin; ATLL-HH, adult T-cell leukemia/lymphoma with HTLV-1-infected HRS-like cells; BM, Bone marrow; Ca, calcium; f, focal (10%-30% of cells positive); F, female; LDH, lactate dehydrogenase; M, male; MC, mixed cellularity; NA, not assessed; NE, not evaluable; NS, nodular sclerosis; sIL-2R, soluble interleukin 2 receptor; TRG, TCR-γ chain gene.

**Supplementary Table 1 Clinicopathological characteristics of ATLL-HH, CHL and typical ATLL**

**1B. Clinicopathological characteristics of CHL and typical ATLL**

| Case no. | Clinical characteristics | | | Pathological characteristics | | | |
|---|---|---|---|---|---|---|---|
| | Diagnosis | Age (years)/sex | HTLV-1 antibody | Histology | HBZ-ISH | EBER-ISH | TRG |
| 13 | CHL | 73/F | + | MC | -[b] | +[c] | polyclonal |
| 14[a] | CHL | 61/F | + | MC | -[b] | +[c] | NE |
| 15[a] | CHL | 36/M | - | MC | NA | +[c] | NA |
| 16[a] | CHL | 38/M | - | MC | NA | -[c] | NA |
| 17 | CHL | 40/F | - | NS | NA | -[c] | NA |
| 18[a] | CHL | 28/M | - | NS | NA | -[c] | NA |
| 19[a] | CHL | 78/M | - | MC | NA | +[c] | NA |
| 20 | CHL | 78/M | + | NS | -[b] | +[c] | polyclonal |
| 21 | Typical ATLL | 56/M | + | large anaplastic | NA | NA | NA |
| 22[a] | Typical ATLL | 58/M | + | medium pleomorphic | NA | NA | NA |
| 23[a] | Typical ATLL | 52/F | + | large pleomorphic | NA | NA | NA |
| 24[a] | Typical ATLL | 75/F | + | medium pleomorphic | NA | NA | NA |
| 25[a] | Typical ATLL | 72/F | + | large pleomorphic | NA | NA | NA |
| 26[a] | Typical ATLL | 84/F | + | large pleomorphic | NA | NA | NA |

[a]Validated by immunohistochemistry of CCL17, pSTAT6, TBET, and IDO1.

[b,c]In CHL cases, the evaluation of HBZ-ISH and EBER-ISH was performed on HRS cells.

ATLL, adult T-cell leukemia/lymphoma; CHL, classic Hodgkin lymphoma; F, female; M, male; MC, mixed cellularity; NA, not assessed; NE, not evaluable; NS, nodular sclerosis; TRG, TCR-γ chain gene.

**Supplementary Table 2 Top 30 genes upregulated in ATLL-HH and CHL compared to typical ATLL**

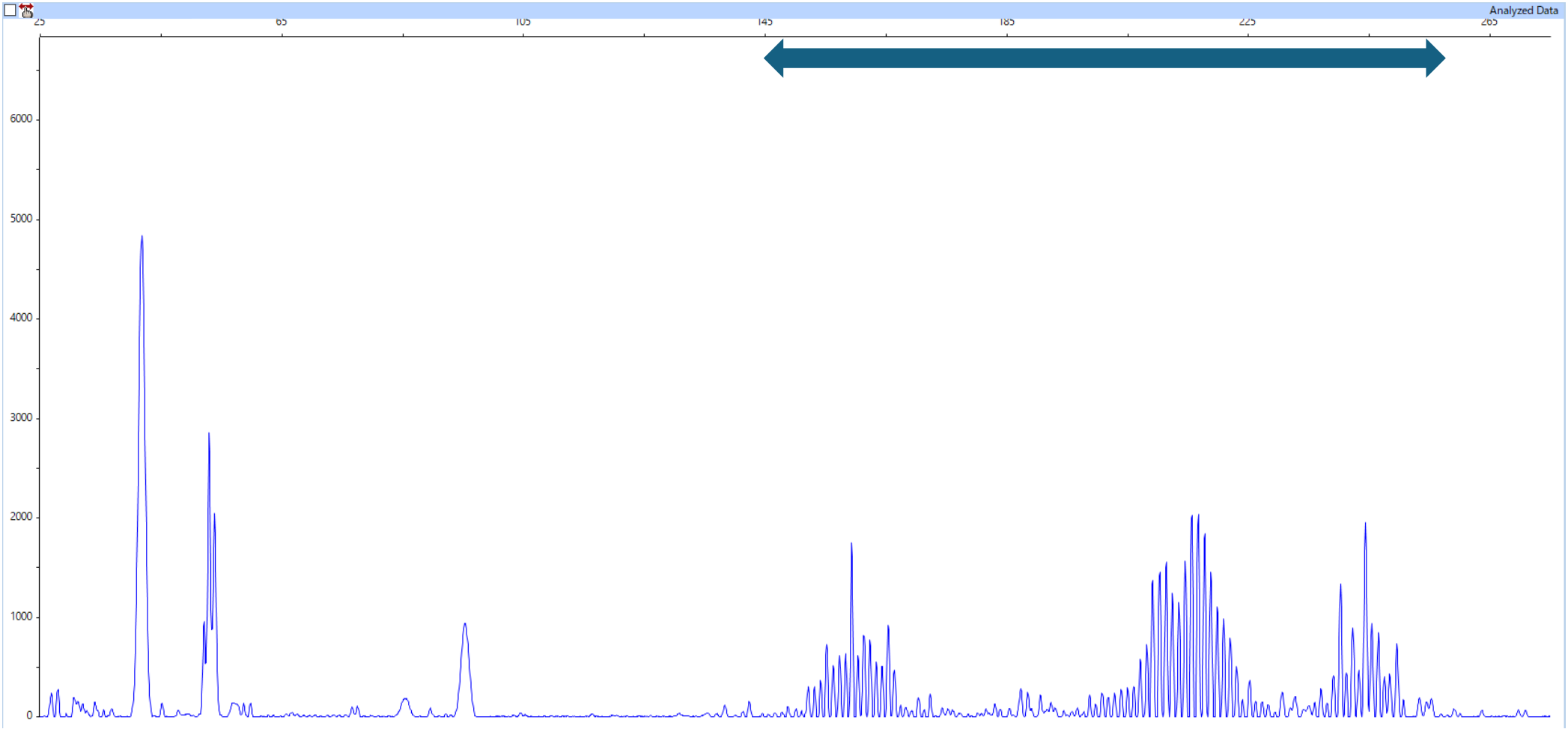
| ATLL-HH | | | CHL | | |
|---|---|---|---|---|---|
| Gene symbol | Log2 fold change | BY.p.value | Gene symbol | Log2 fold change | BY.p.value |
| CXCL9 | 4.76 | 1.82E-05 | S100A8 | 6.28 | 6.21E-05 |
| IL21 | 4.64 | 6.32E-07 | KLRB1 | 4.78 | 3.11E-05 |
| CXCL13 | 4.42 | 0.00013 | CD7 | 3.69 | 2.67E-08 |
| CHIT1 | 4.36 | 0.000461 | CXCR6 | 3.53 | 1.59E-06 |
| KLRB1 | 4.23 | 3.12E-05 | SLAMF1 | 3.44 | 1.59E-06 |
| HSD11B1 | 4.11 | 6.11E-06 | CCR5 | 3.31 | 2.51E-06 |
| HAMP | 4.03 | 0.00129 | CXCR3 | 3.1 | 2.44E-06 |
| C4B | 3.94 | 7.02E-06 | SLAMF7 | 2.99 | 2.33E-05 |
| CR2 | 3.8 | 0.0041 | TLR2 | 2.79 | 1.52E-05 |
| SLAMF7 | 3.79 | 2.16E-07 | TNFSF13 | 2.54 | 4.14E-05 |
| GZMH | 3.76 | 1.83E-05 | TNFSF8 | 2.54 | 6.23E-05 |
| TLR8 | 3.72 | 1.61E-06 | CSF2RB | 2.53 | 3.20E-06 |
| CD7 | 3.56 | 6.44E-09 | MAF | 2.5 | 5.95E-06 |
| CXCR6 | 3.52 | 2.07E-07 | CSF1R | 2.41 | 1.52E-05 |
| CCR5 | 3.51 | 2.14E-07 | HCK | 2.36 | 1.51E-05 |
| SLAMF1 | 3.47 | 2.07E-07 | LYN | 2.36 | 1.82E-05 |
| CCL17 | 3.47 | 0.00785 | CD40 | 2.32 | 3.58E-06 |
| S100A8 | 3.44 | 0.00982 | CD84 | 2.3 | 2.48E-06 |
| IFNG | 3.4 | 8.04E-07 | CYBB | 2.3 | 1.33E-05 |
| CCL18 | 3.28 | 0.0188 | TLR4 | 2.25 | 1.33E-05 |
| C1QB | 3.25 | 3.31E-05 | CCR2 | 2.1 | 3.11E-05 |
| CXCR3 | 3.24 | 2.14E-07 | CMKLR1 | 1.99 | 3.71E-05 |
| IDO1 | 3.24 | 3.66E-05 | ICAM1 | 1.94 | 1.67E-05 |
| CXCL11 | 3.13 | 0.00159 | STAT4 | 1.89 | 1.59E-06 |
| LILRB1 | 3.12 | 1.89E-06 | IRF8 | 1.86 | 4.41E-05 |
| POU2AF1 | 3.07 | 0.000348 | LTBR | 1.86 | 6.21E-05 |
| IL6 | 3.06 | 0.00472 | TLR1 | 1.82 | 1.67E-05 |

| | | | | | |
|---|---|---|---|---|---|
| TNFSF8 | 3.05 | 1.31E-06 | IL10RA | 1.76 | 2.06E-05 |
| CXCL10 | 3.04 | 0.00433 | PRKCD | 1.32 | 4.75E-05 |
| CCL23 | 3.03 | 0.0462 | RELB | 1.25 | 3.26E-05 |

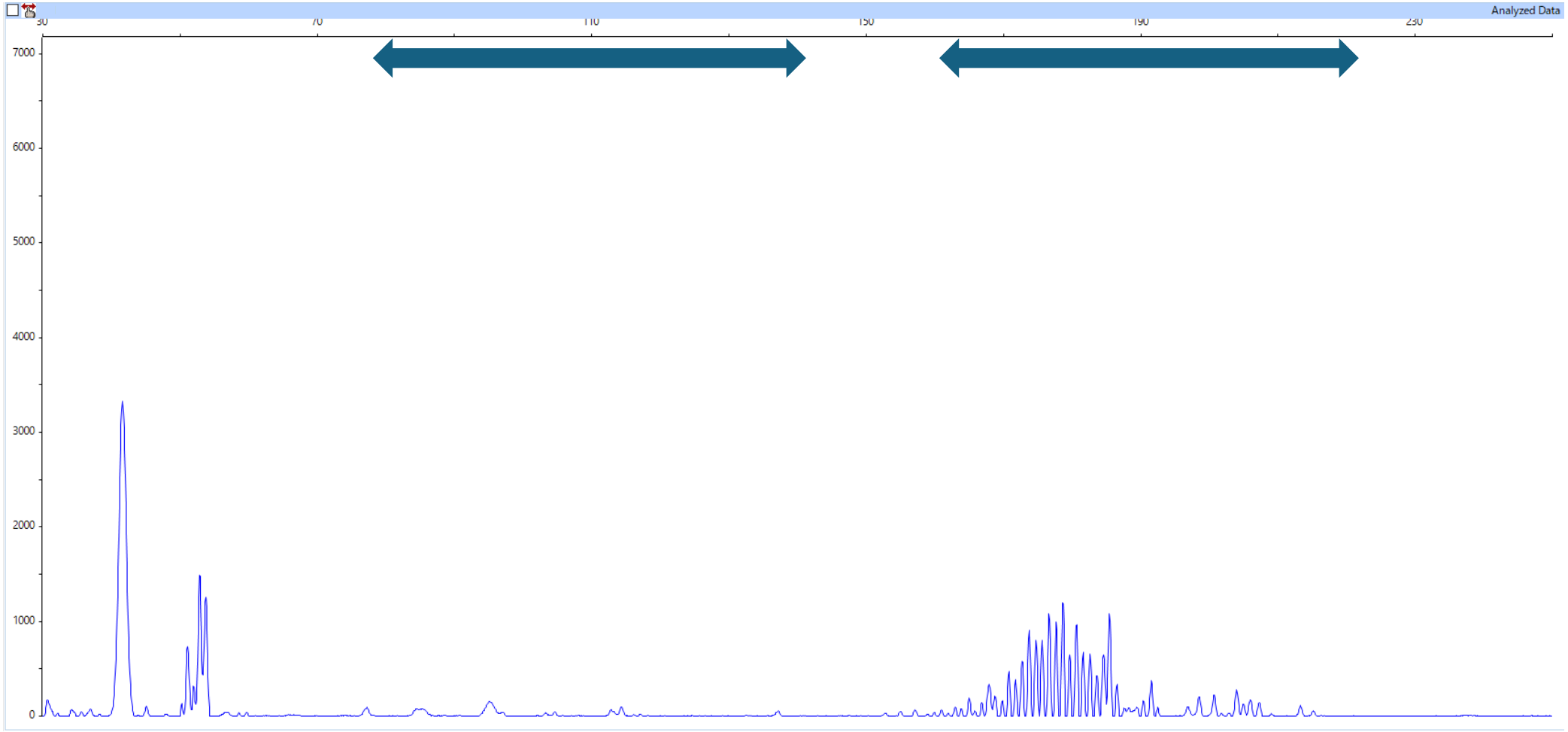
ATLL-HH, adult T-cell leukemia/lymphoma with HTLV-1-infected HRS-like cells; CHL, classic Hodgkin lymphoma; ATLL, adult T-cell leukemia/lymphoma.

**Supplementary Figure 1 TRG clonality assay of ATLL-HH.**
The X-axis indicates the size of the amplicons, and the Y-axis indicates fluorescent signal intensity. The blue arrow shows the size range of the amplicons that can be evaluated.

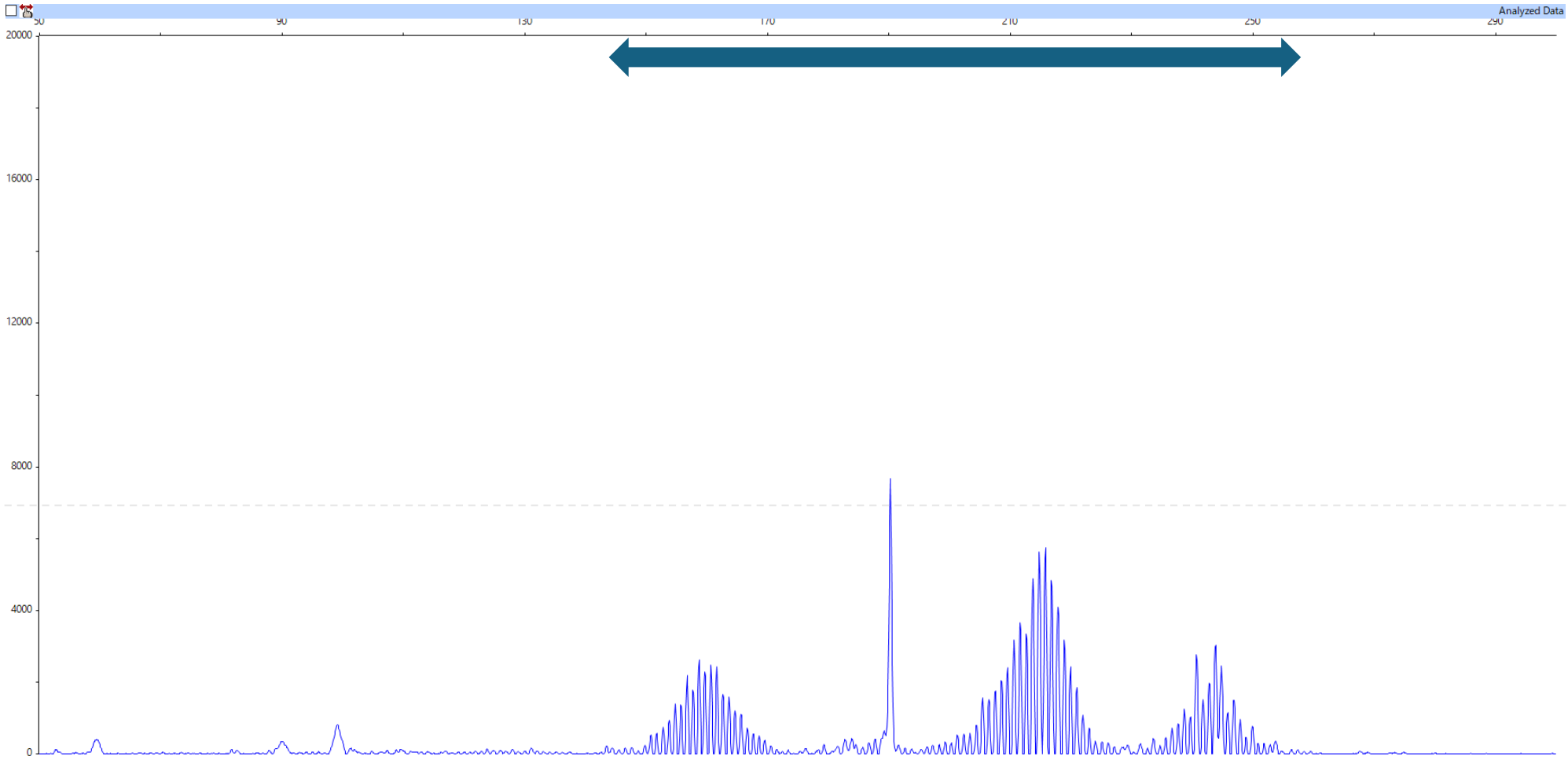
# case 1 TRG(A)


Analyzed Data
25
65
105
145
185
225
265
6000
5000
4000
3000
2000
1000
0

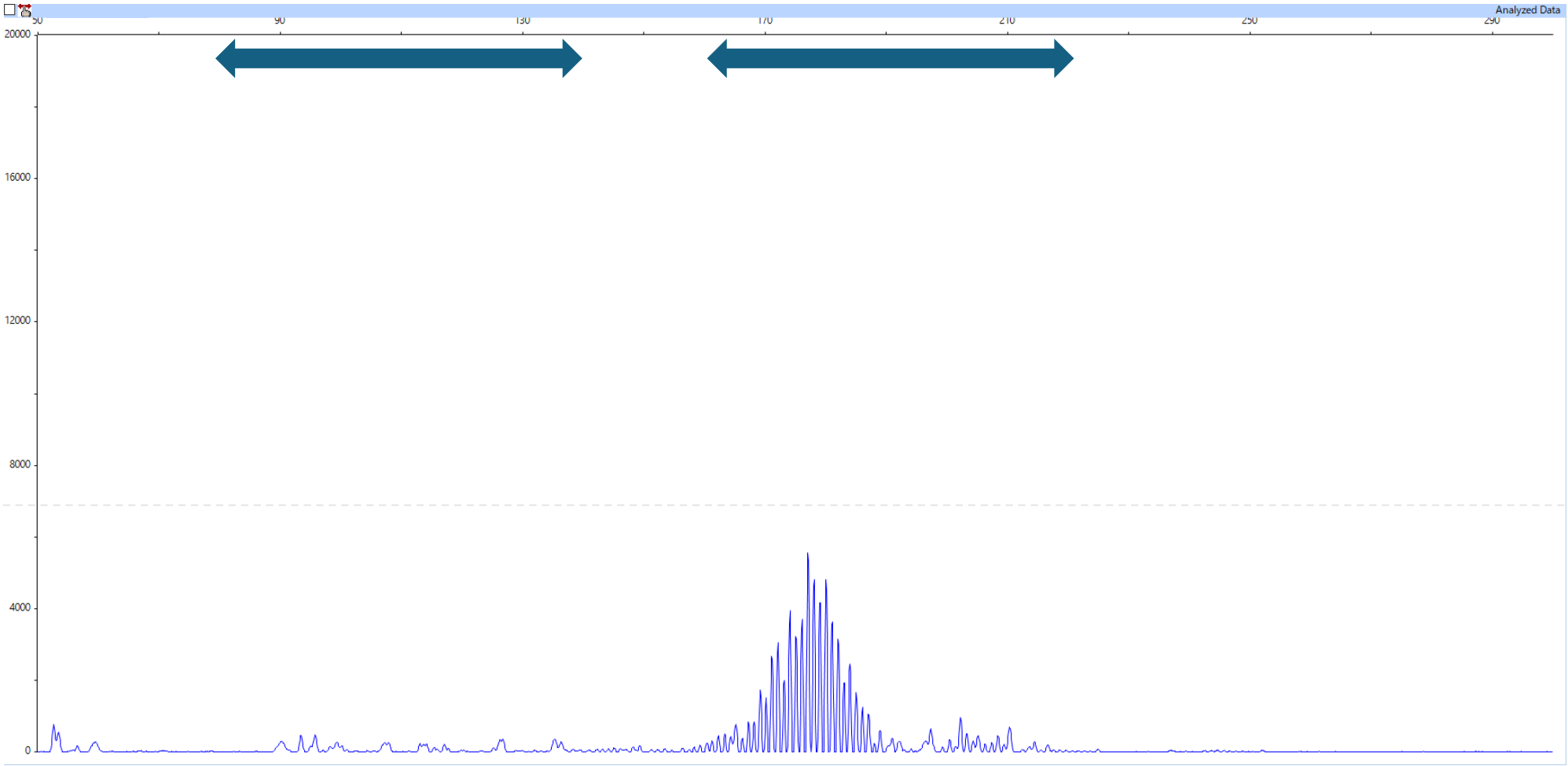
# case 1 TRG(B)


Analyzed Data
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150
190
230
7000
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5000
4000
3000
2000
1000
0

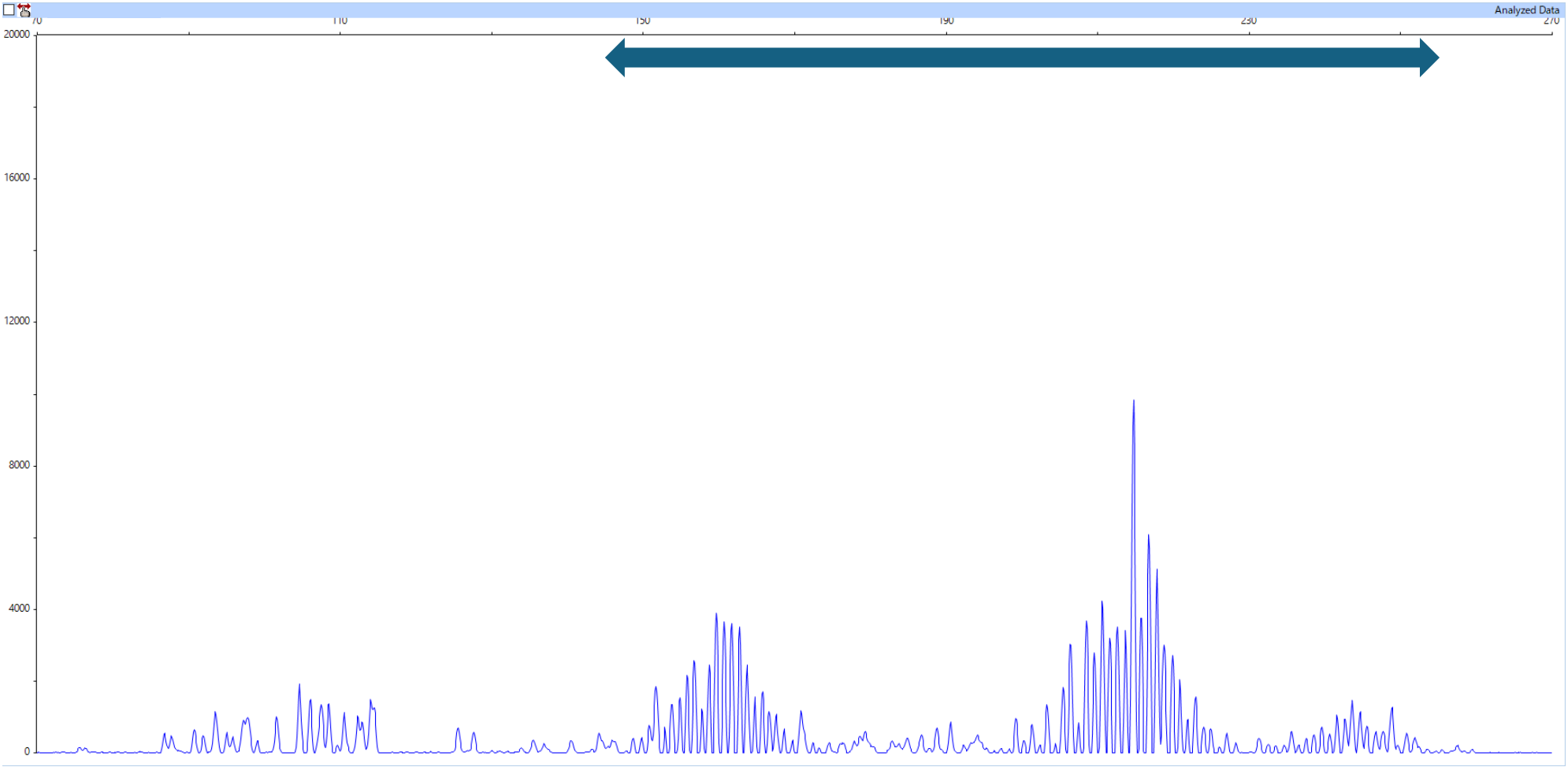
# case 3 TRG(A)


Analyzed Data
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170
210
250
290
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4000
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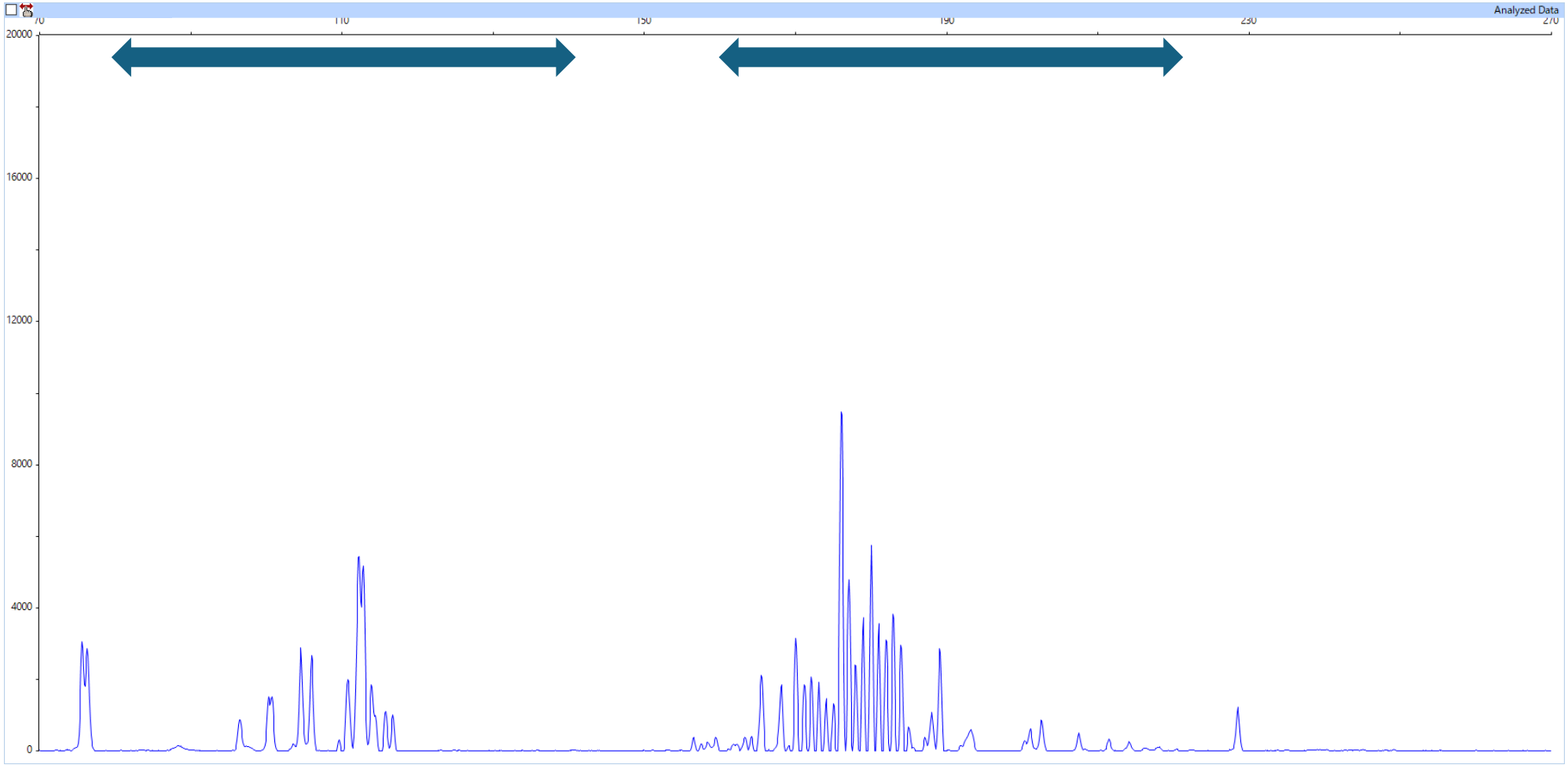
# case 3 TRG(B)


Analyzed Data
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130
170
210
250
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12000
8000
4000
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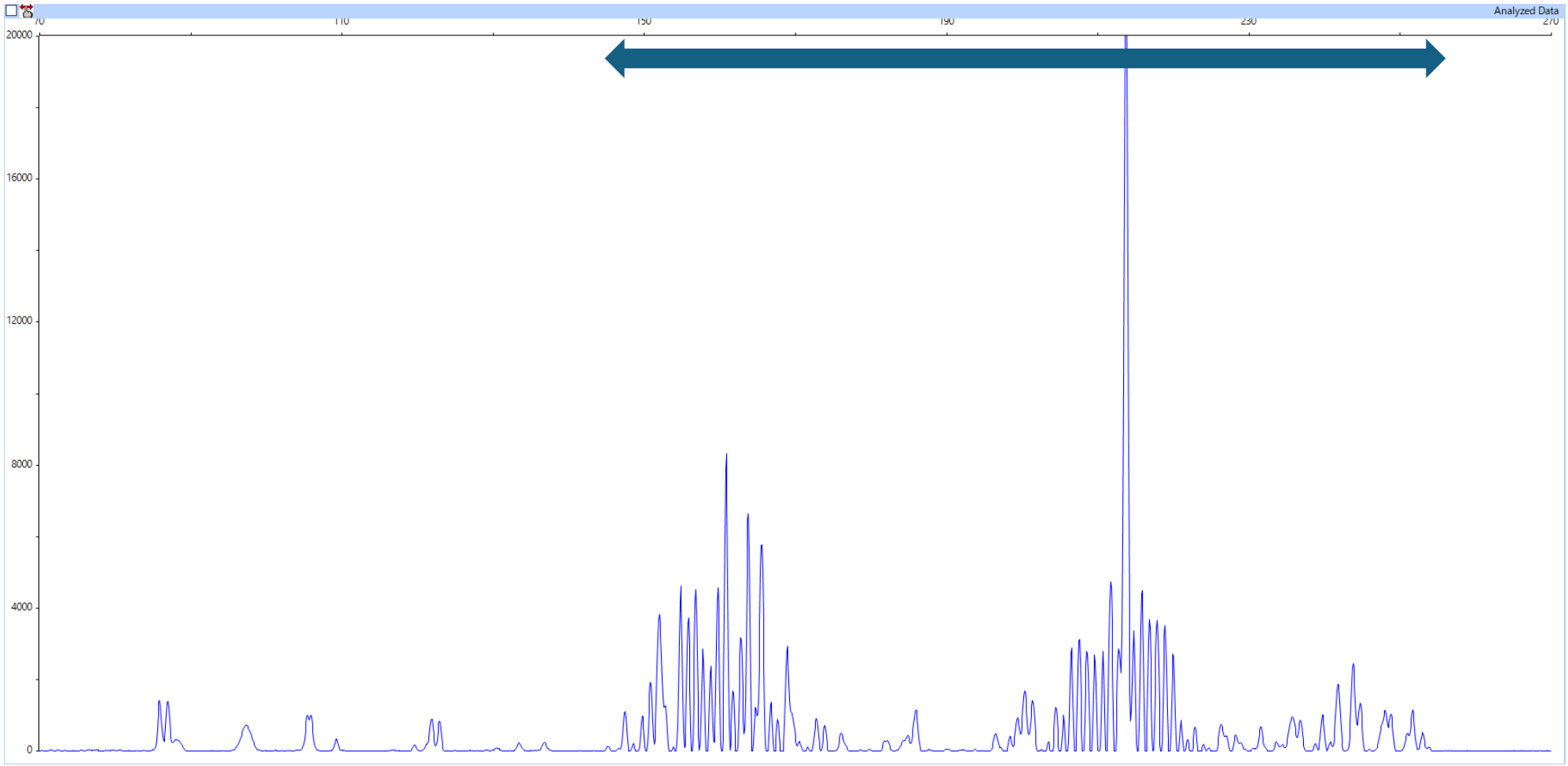
# case 4 TRG(A)


Analyzed Data
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150
190
230
270
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8000
4000
0

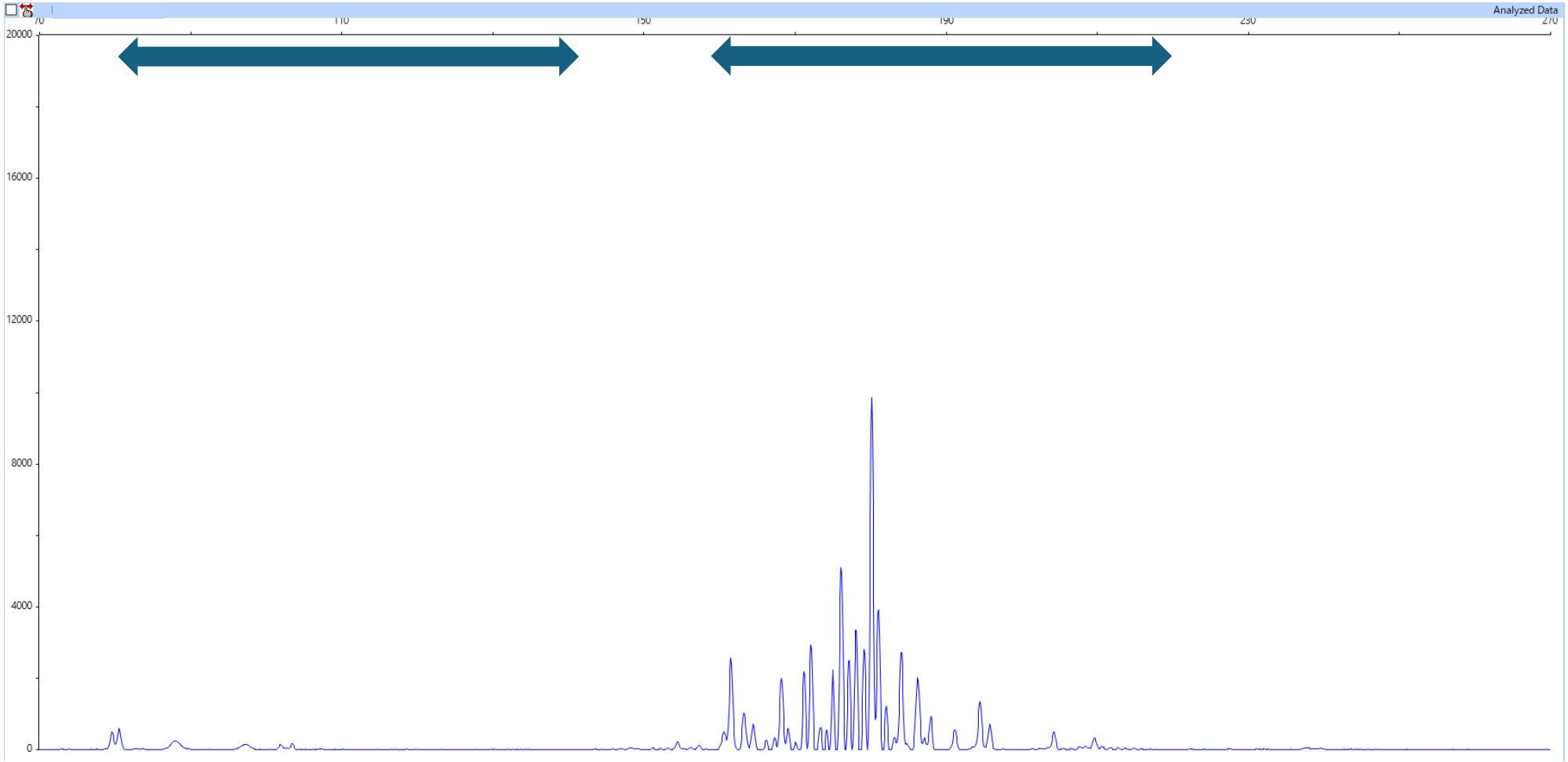
# case 4 TRG(B)


Analyzed Data
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190
230
270
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8000
4000
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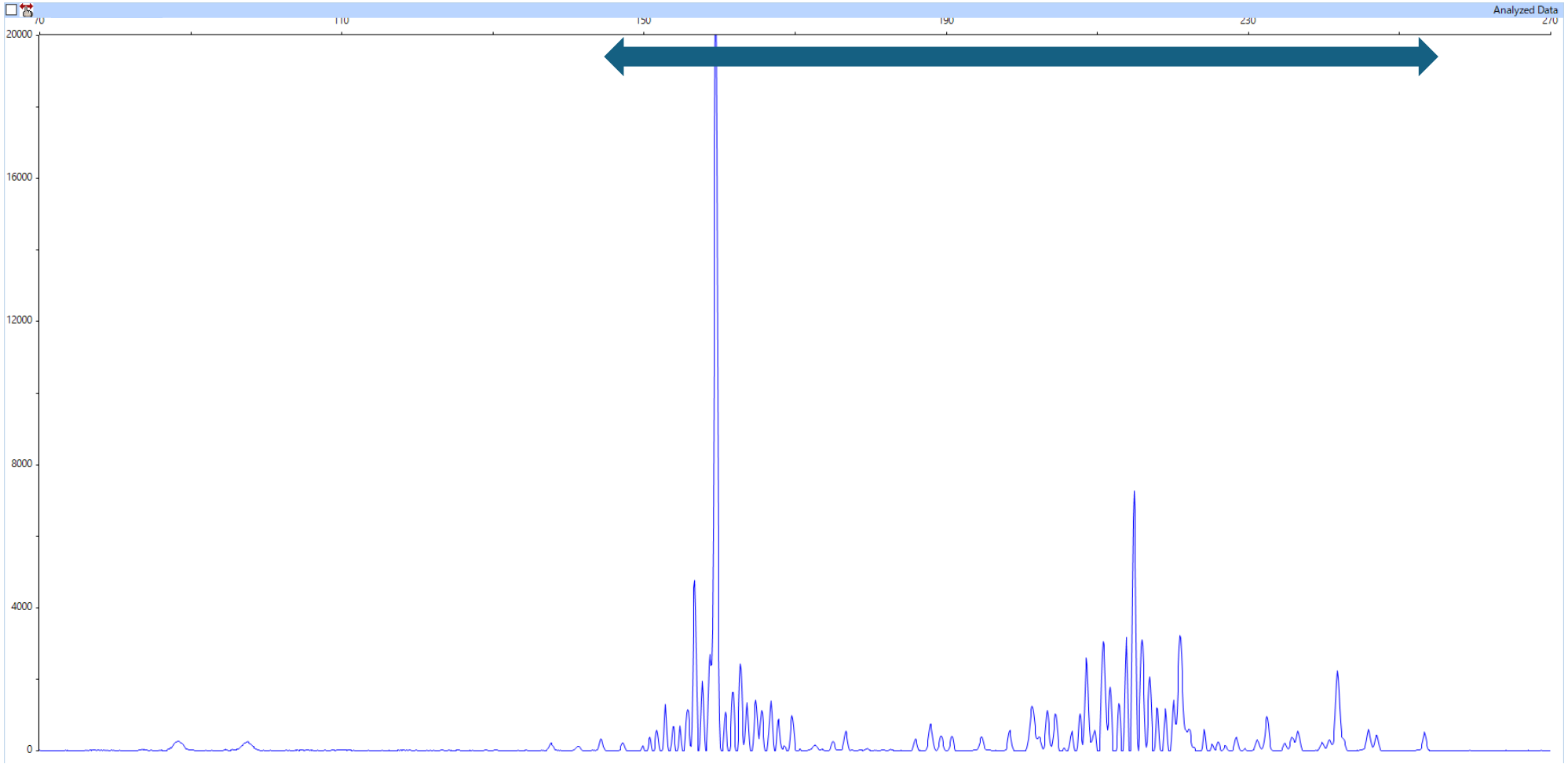
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150
190
230
270
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16000
12000
8000
4000
0

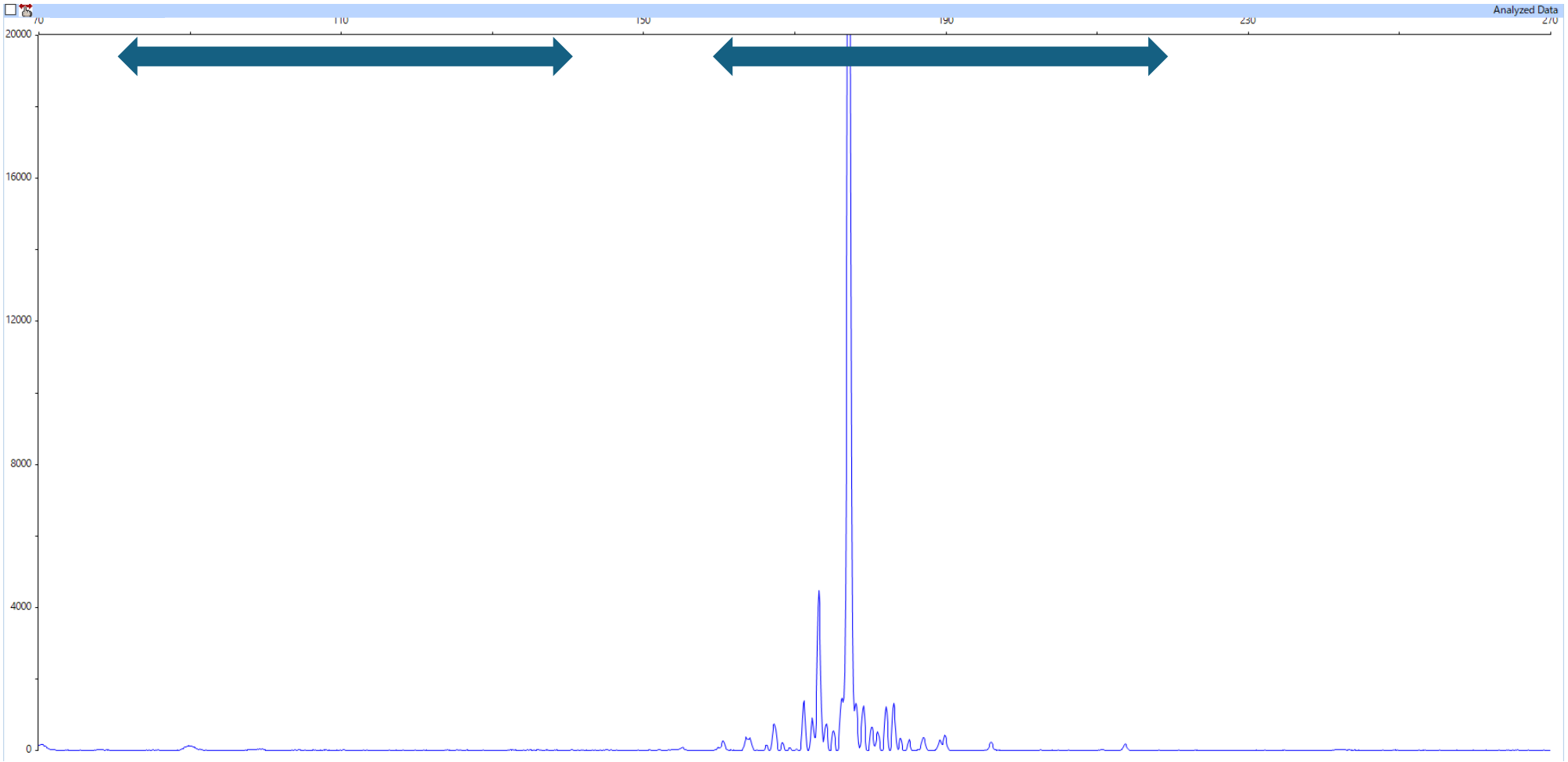
# case 6 TRG(B)


Analyzed Data
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110
150
190
230
270
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16000
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8000
4000
0

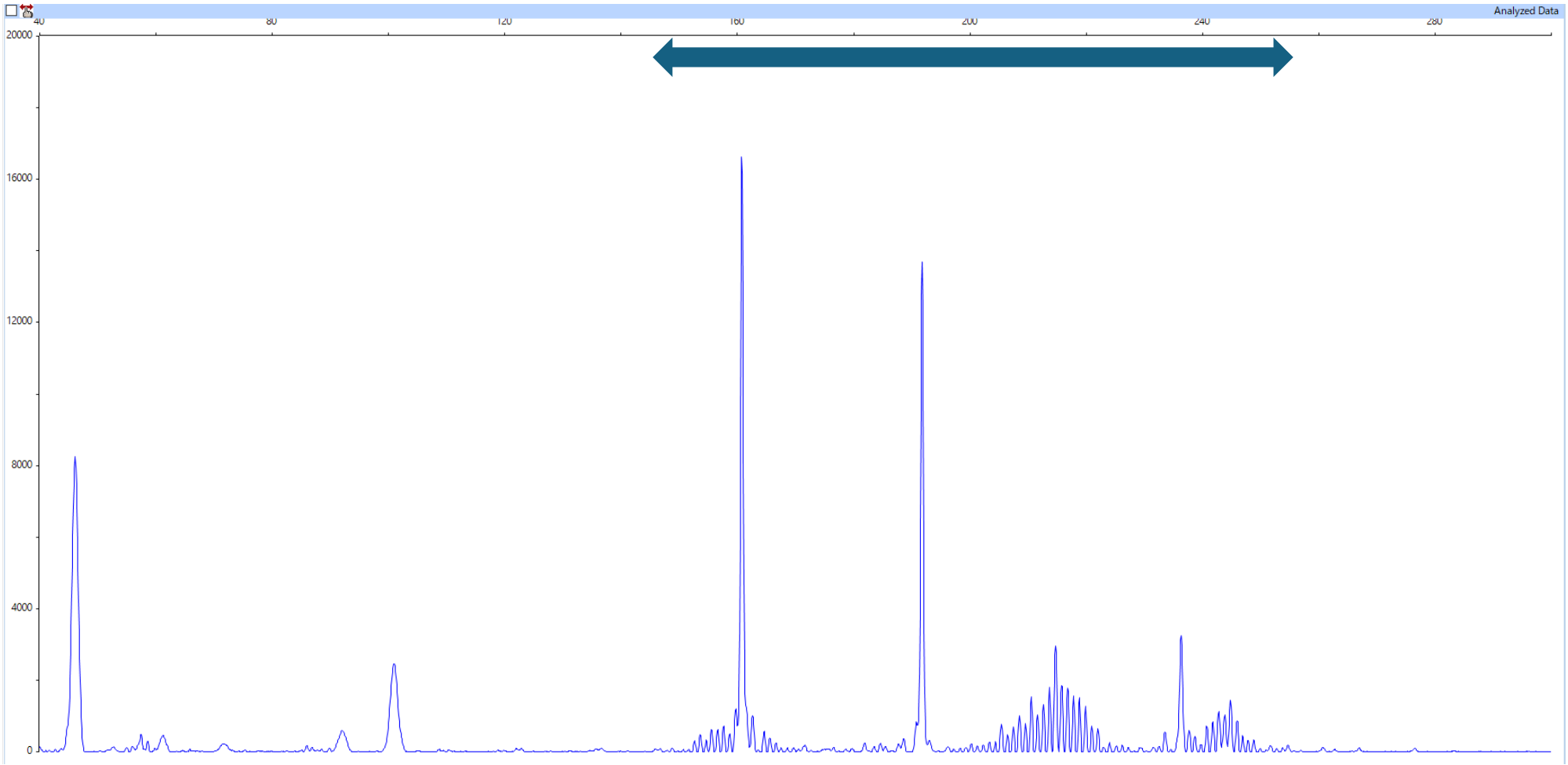
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Analyzed Data
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110
150
190
230
270
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8000
4000
0

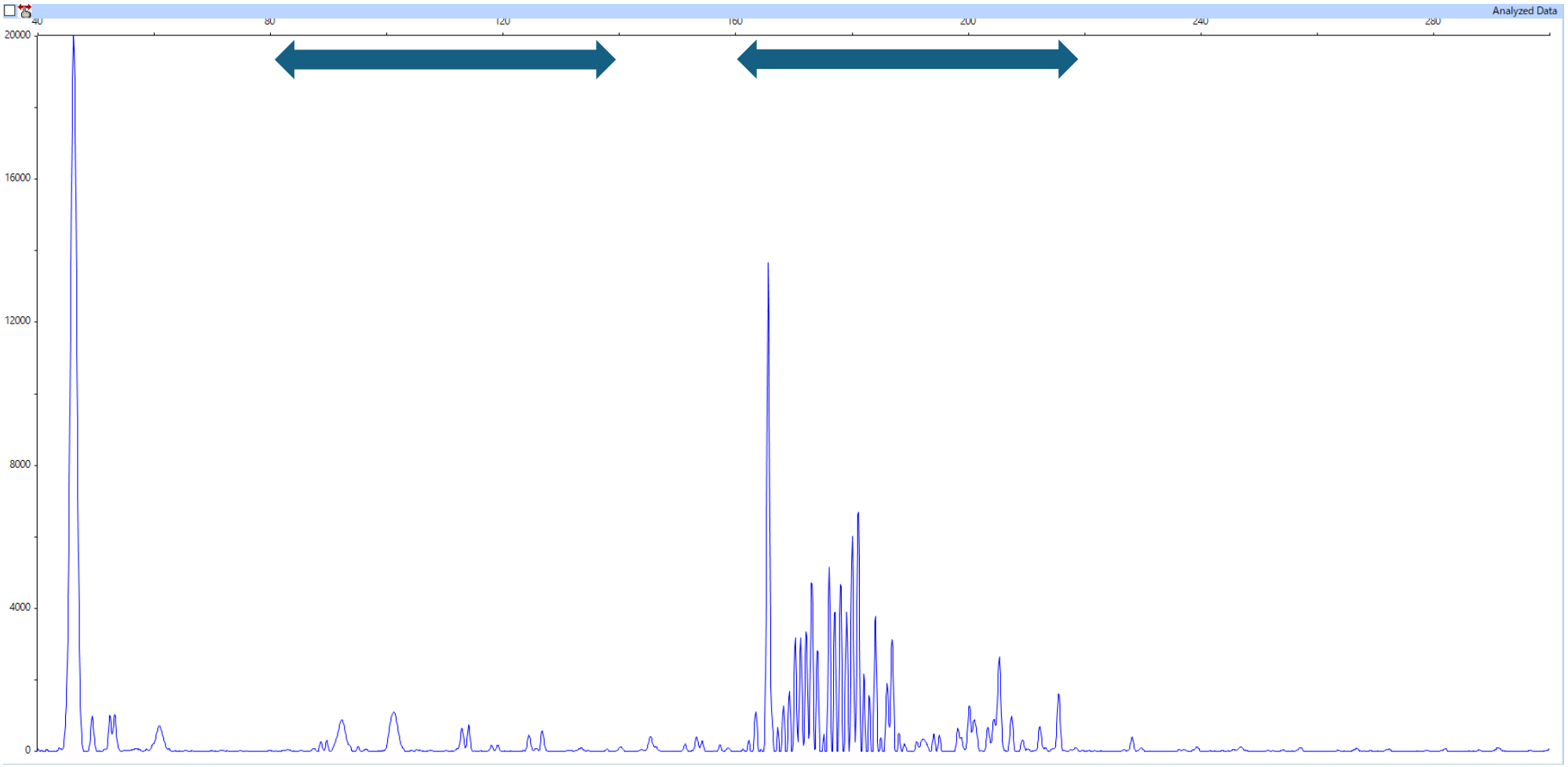
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Analyzed Data
70
110
150
190
230
270
20000
16000
12000
8000
4000
0

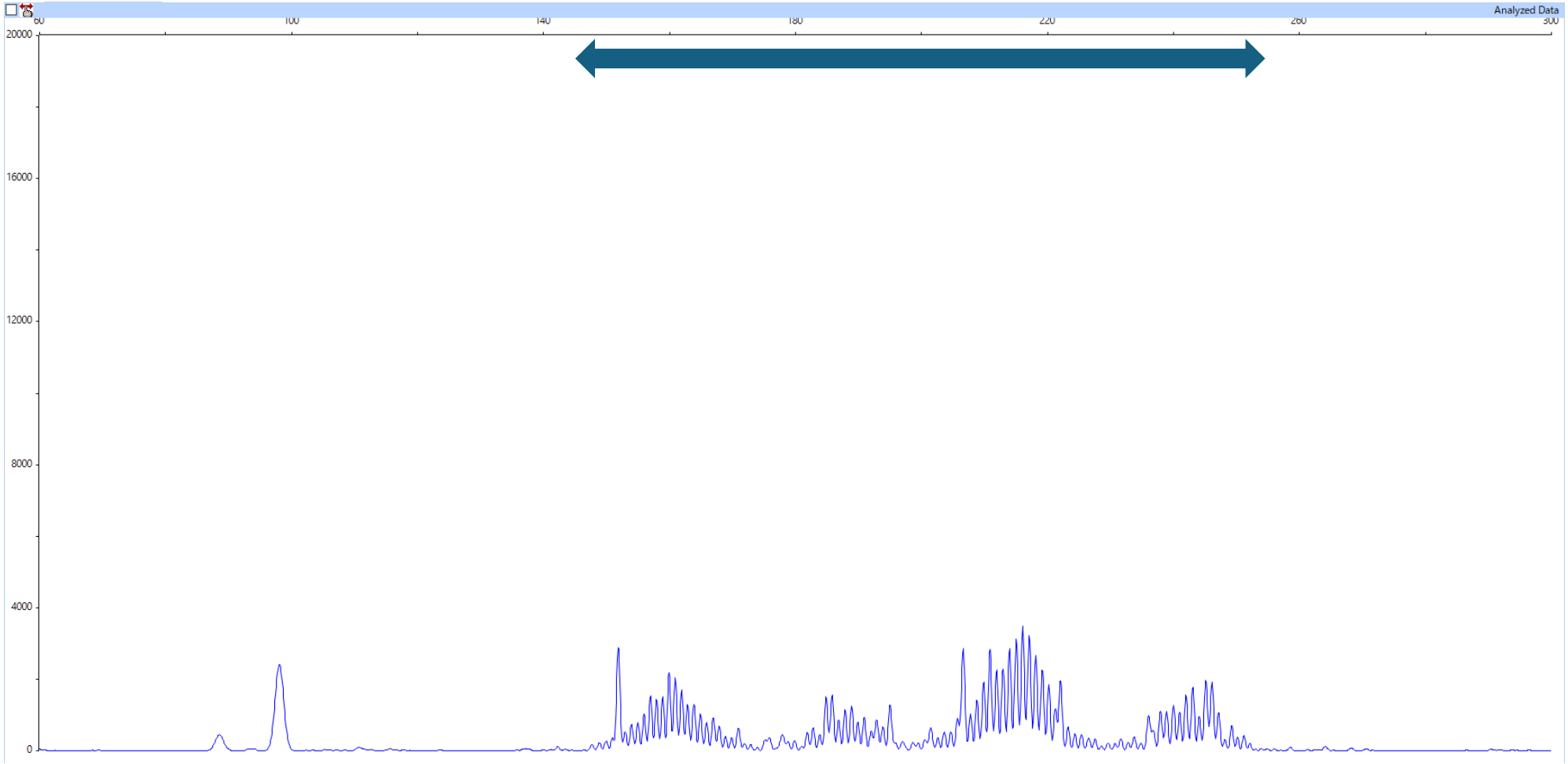
# case 8 TRG(A)


Analyzed Data
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80
120
160
200
240
280
20000
16000
12000
8000
4000
0

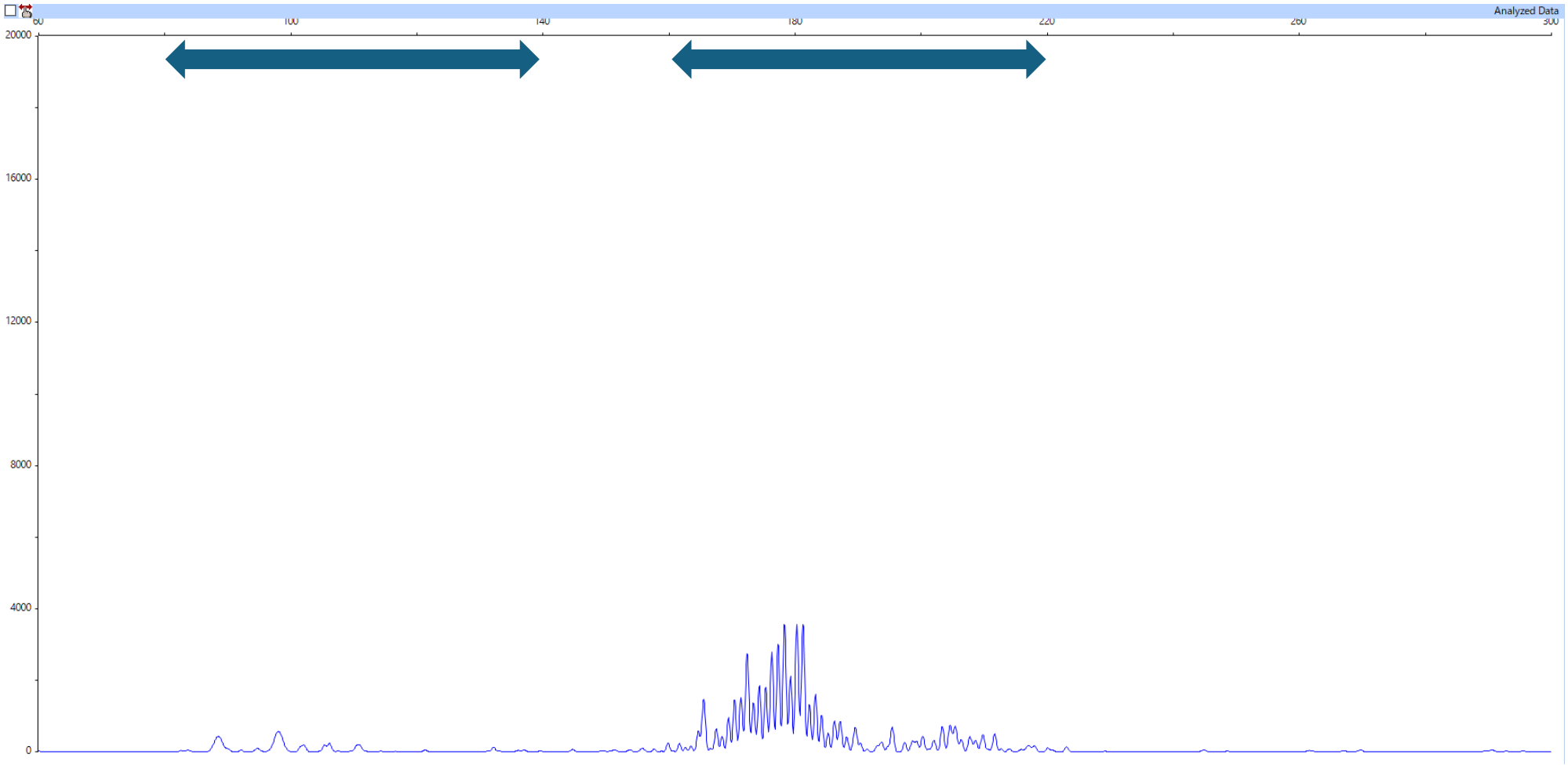
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Analyzed Data
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200
240
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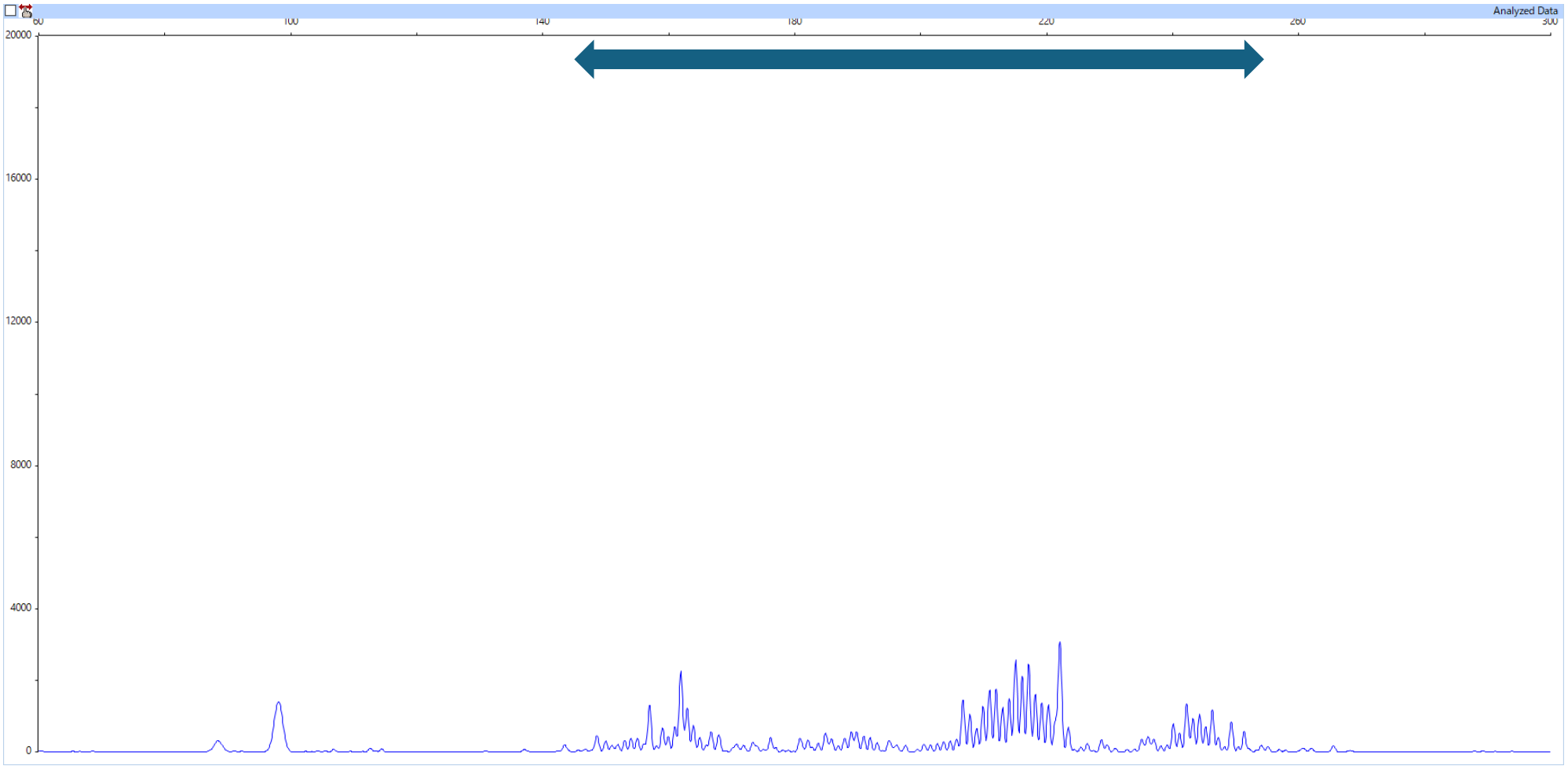
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Analyzed Data
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180
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12000
8000
4000
0

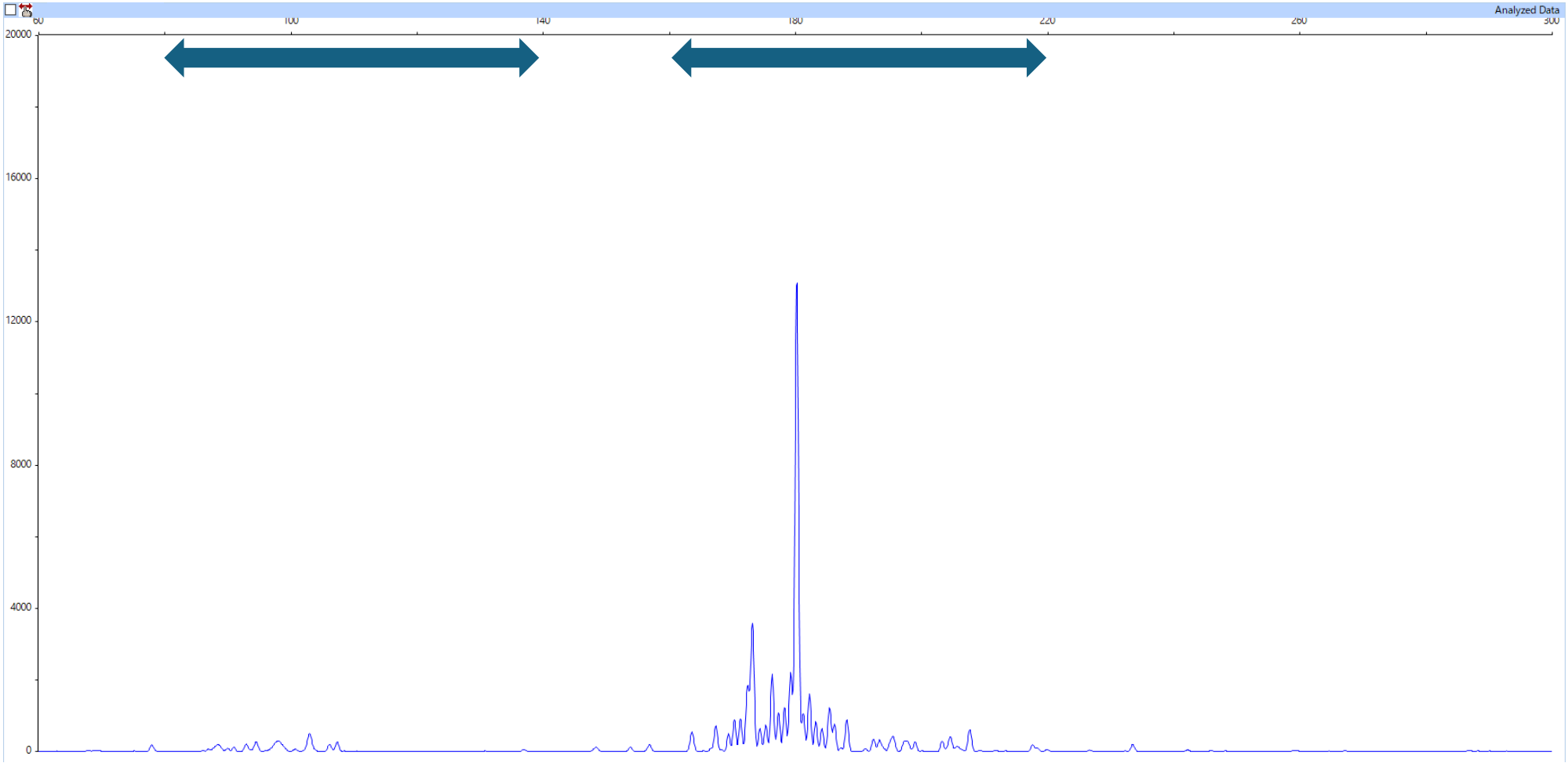
# case 9 TRG(B)


Analyzed Data
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100
140
180
220
260
300
20000
16000
12000
8000
4000
0

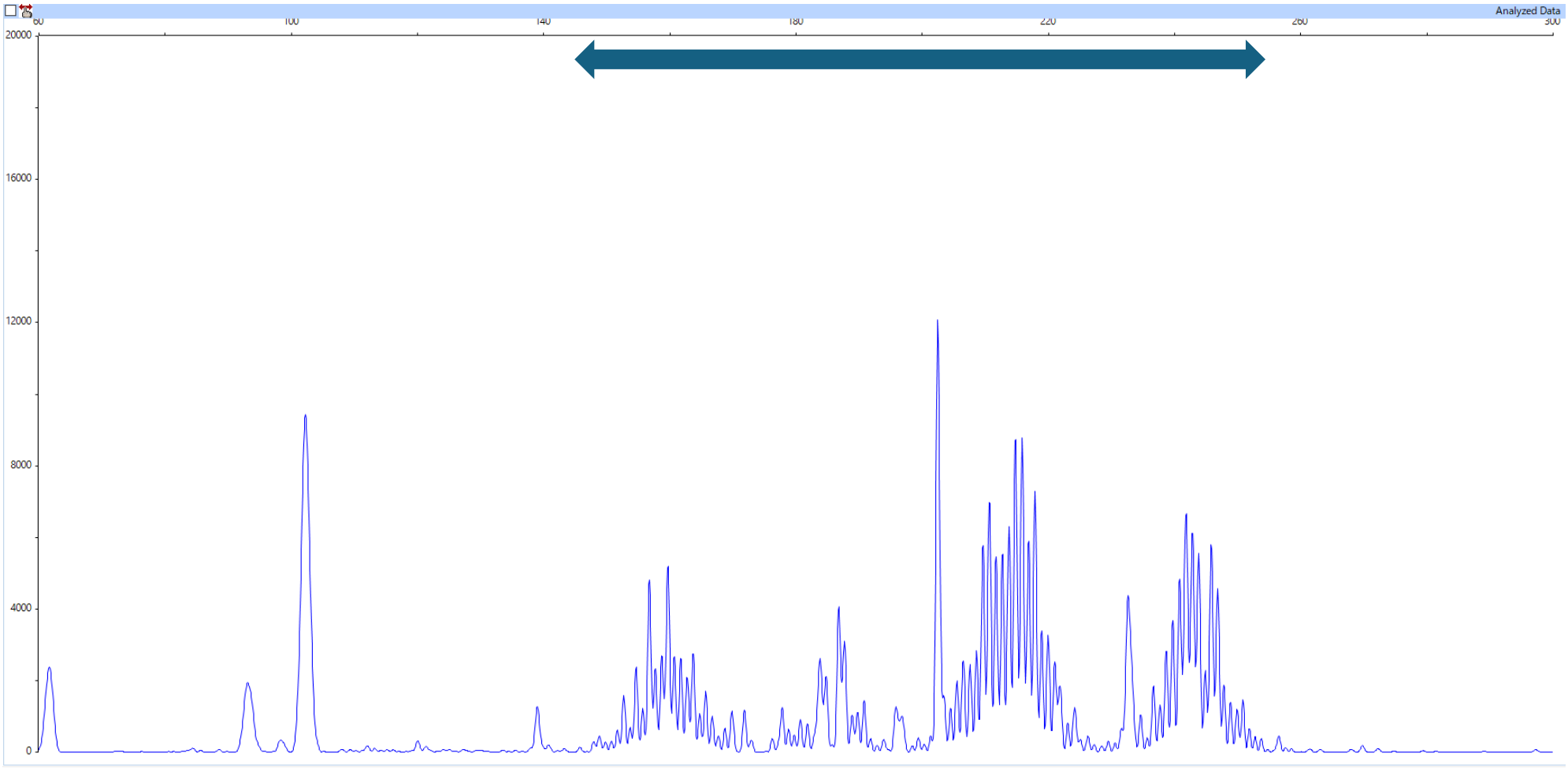
# case 10 TRG(A)


Analyzed Data
60
100
140
180
220
260
300
20000
16000
12000
8000
4000
0

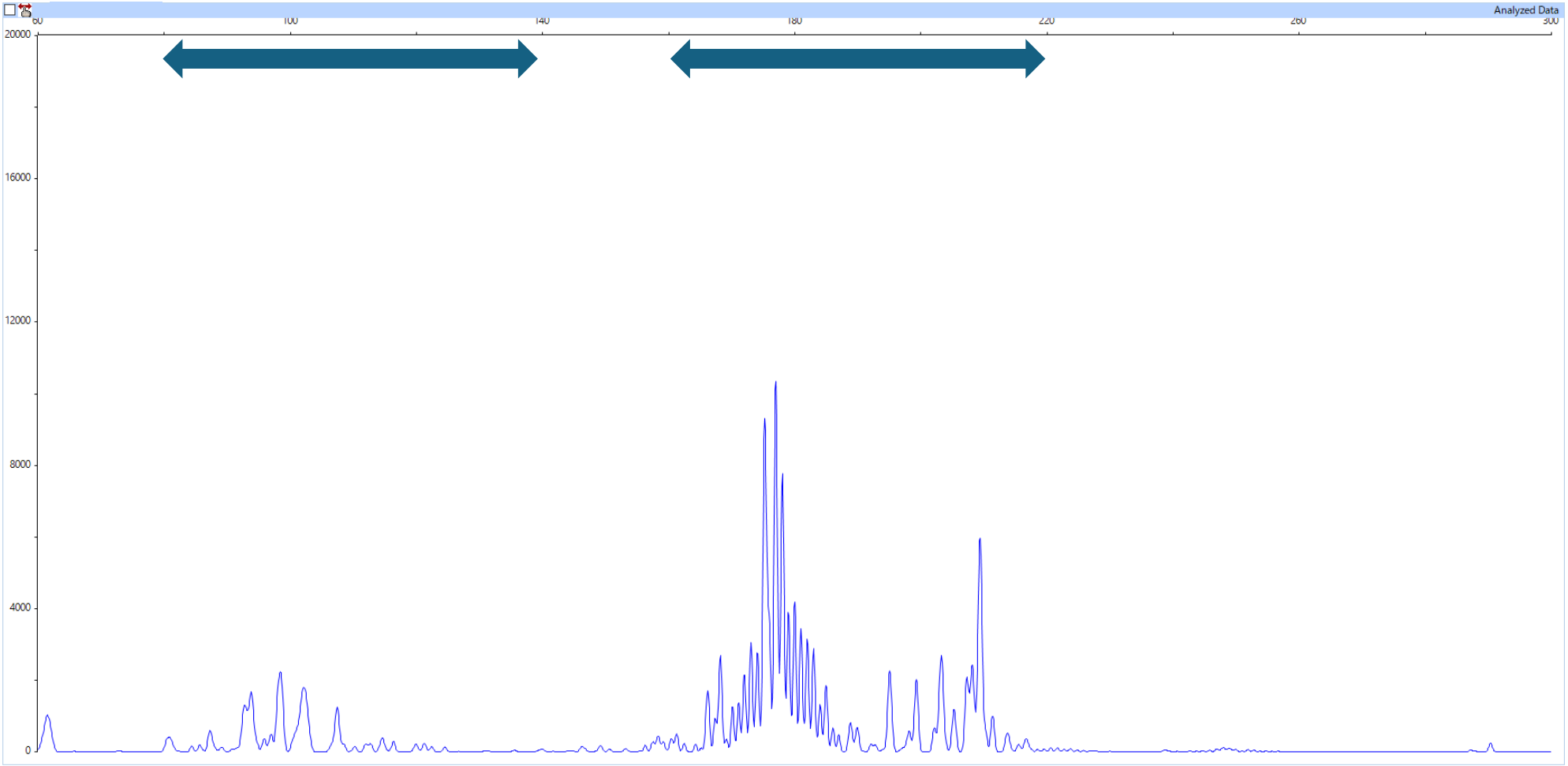
# case 10 TRG(B)


Analyzed Data
60
100
140
180
220
260
300
20000
16000
12000
8000
4000
0

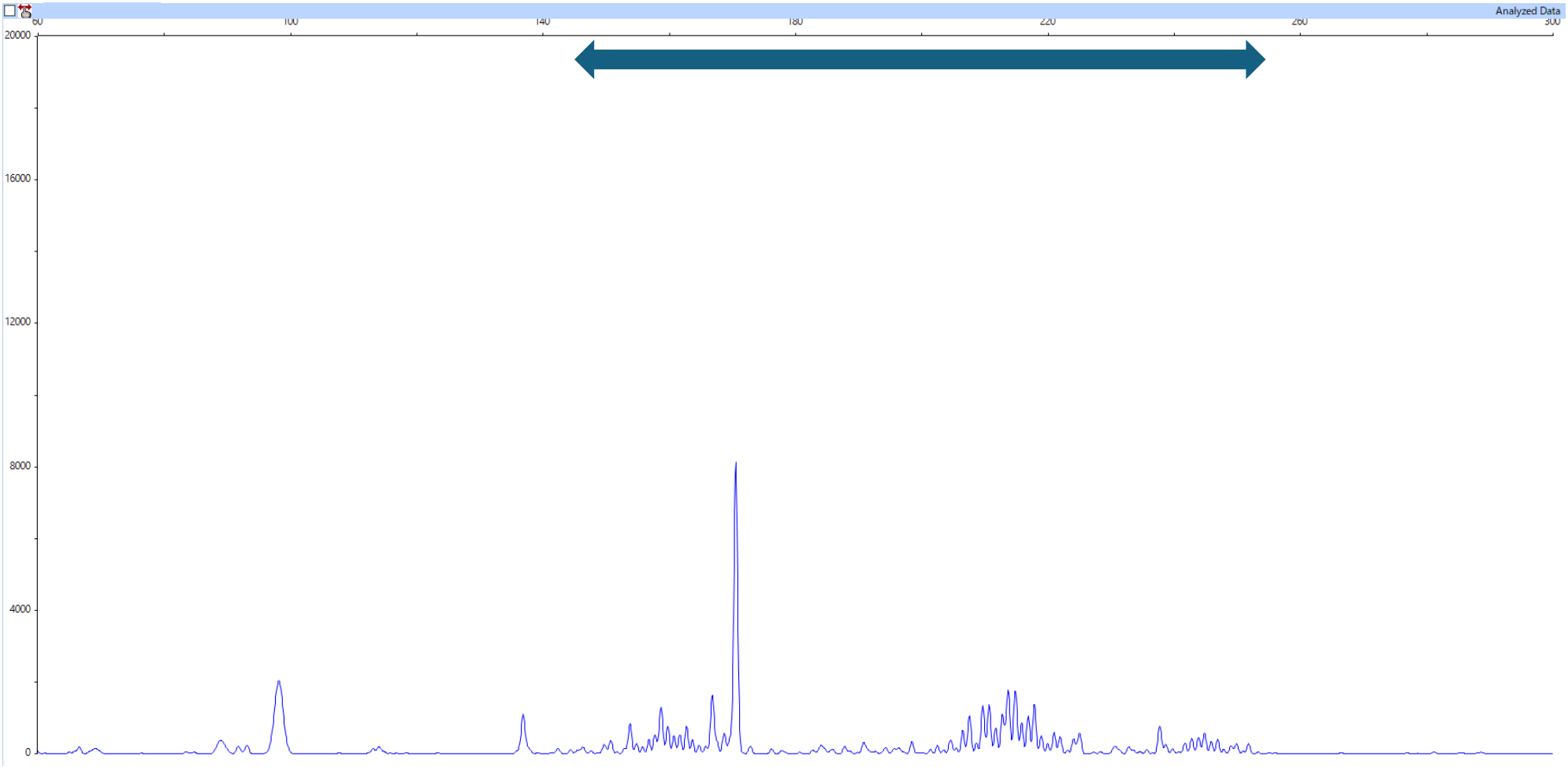
# case 11 TRG(A)


Analyzed Data
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100
140
180
220
260
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20000
16000
12000
8000
4000
0

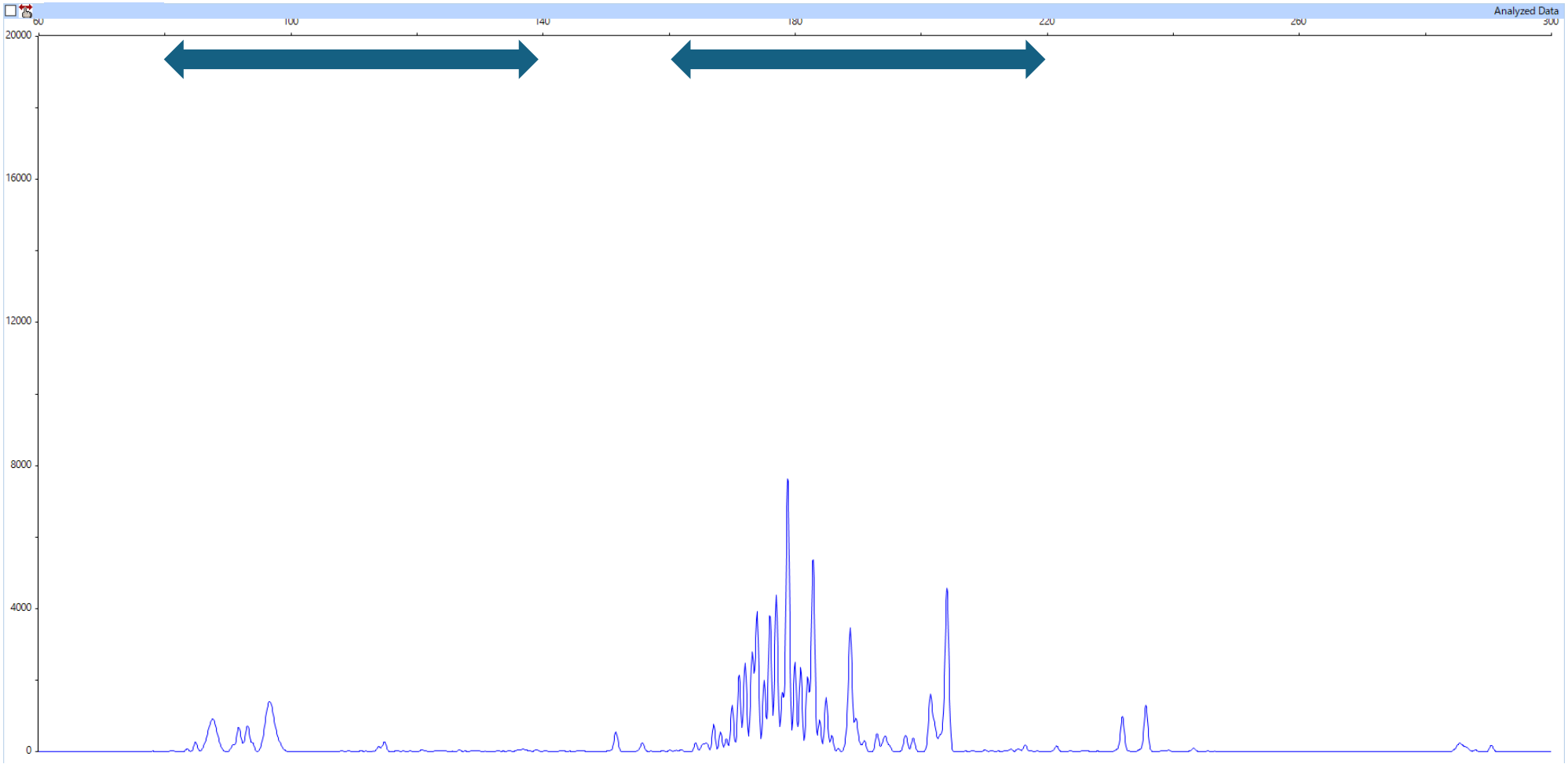
# case 11 TRG(B)


Analyzed Data
60
100
140
180
220
260
300
20000
16000
12000
8000
4000
0

# case 12 TRG(A)


Analyzed Data
60
100
140
180
220
260
300
20000
16000
12000
8000
4000
0

# case 12 TRG(B)


Analyzed Data
60
100
140
180
220
260
300
20000
16000
12000
8000
4000
0